INFLAMMATION OF THE BLADDER
AND
URINARY FEVER

C. W. MANSELL MOULLIN

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AND

URINARY FEVER

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PREFACE.

Only a few words seem to me to be needed to explain my reasons for writing this book. It does not appear to be admitted everywhere as a matter of common knowledge and beyond dispute, that inflammation of the bladder is always due to micro-organisms, which in the vast majority of instances have invaded it from without; and that what is commonly called urinary fever is nothing but septic intoxication or septic infection occurring under special conditions. The principles of aseptic surgery seem still to stand in need of an advocate when the bladder is concerned; and it seems to be still necessary to insist upon the fact that catheters are always septic unless they have been thoroughly sterilised. My attention was forcibly drawn to this subject some years ago while I was engaged in preparing the Hunterian Lectures on the Operative Treatment of Enlargement of the Prostate, by noticing the strange confusion that existed as to the relationship between inflammation of the bladder and the decomposition of urea; and I began then a series of observations upon cystitis and urinary fever which have been continued at intervals, as time and the pressure of other work allowed, and which now I have at length been able to put together in their present form.

C. MANSELL MOULLIN.

69 WIMPOLE STREET, W.
March, 1898.

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INFLAMMATION OF THE BLADDER

AND

URINARY FEVER.

CERTAIN ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS IN CONNECTION WITH INFLAMMATION OF THE BLADDER.

I do not consider it either necessary or advisable, in a work of this kind, to enter into the general question of the anatomy and physiology of the bladder. The subject is dealt with thoroughly in the various textbooks devoted to the purpose. An exception may, however, I think, be made in favour of a few points, that have a direct and somewhat important bearing upon the relations that exist between the walls of the bladder and the organisms that invade it.

The epithelium of the bladder. The epithelium lining the bladder is transitional in character, and arranged in several strata. The lowest cells are oval or rounded. The next are pear shaped, with the narrower end running down between the deeper cells. The most superficial are cubical, but hollowed out upon their under surface, where they rest upon those below. The shape, however, differs considerably, according to the method of preparation, and the degree to which the bladder was distended before being hardened. In the infant, if microscopic sections are made through the bladder wall near the orifice, the superficial cells are of the same columnar shape as those that line the urethra. Normally, in the adult, the flatter cells can be traced some little distance from the bladder, down the urethra, before they are replaced by cylindrical ones. But the line of transition is very irregular, the prominences in the urethra being covered by flatter cells, while the depressions between them retain those of columnar shape. All the cells in the bladder, whatever their shape, are connected with each other by cell-bridges, as in the epidermis.

Absorption from the bladder. The function of the epithelial lining is entirely protective. So long as the surface is uninjured, there is no absorption from the bladder. In this respect the epithelium is almost as impermeable as the epidermis, although, of course, much more delicate in structure, and more easily injured.

At first sight, it does not appear that there could be any difficulty in determining by experiment the simple question, whether absorption can or cannot take place in a healthy bladder. Yet the results that have been obtained are most contradictory. Probably the same conditions were not strictly observed. Kuss and Duval, for instance, experimenting upon the bladder after death, denied that there was any absorption, so long as the epithelium was intact, and only a short time had been allowed to elapse. This was confirmed by Susini (Guyon, *Leçons Cliniques*, tome ii., p. 145) who showed that the same held good during life, both in the case of the human bladder and that of animals ; and by Boyer and Guinard (*Arch. de Med. Experiment. et d'Anat. Path.*, tome vi., 206, p. 813, 1894) who experimented upon dogs with cocaine and morphia, and proved that if the bladder was healthy and contained a little urine, these substances were not absorbed.

On the other hand Bazy and Sabatier, using stronger solutions, and injecting them into a healthy bladder, obtained exactly the opposite results.

Some of the experiments performed on rabbits by Bazy (*Soc. de Biologie*, July 28, 1894) are especially valuable. Cultures of the pneumococcus injected into the bladder were followed by pleurisy and peritonitis, and proved rapidly fatal without any renal lesion. The same result followed if the products of the septic decomposition of albumin were separated off by Chamberland's filter and injected; or a culture of the bacillus pyocyaneus sterilised by heat. And not only liquid products, but even gases, according to the same authority, can be absorbed. Oxygen, at any rate, if injected into the bladder, disappears from it, and bubbles of gas can be seen in the blood vessels.

The best explanation for these conflicting results is that suggested by Boyer and Guinard (*Soc. de Biologie*, June 18, 1894). They found that although a single injection was not followed by absorption (unless the solution used was highly concentrated), a second, made a few days later, usually was. Sufficient allowance has not been made, hitherto, for the effect that alkaloids and concentrated solutions exert upon the epithelial cells. Anything that injures the cells, or impairs their vitality, destroys their protecting power, and renders absorption possible.

It is noteworthy that according to Brieger (Gautier, *Les Toxines*, p. 85) putrescine and cadaverine, two of the ptomaines that are found among the products of the growth of the bacterium coli, are capable of causing necrosis of the intestinal epithelium. If they have the same effect upon the vesical cells this may help to explain the rapidity with which the products of septic decomposition were absorbed in Bazy's experiments.

The question as to the possibility of absorption from the bladder, when the surface is inflamed, turns upon the same point, the extent to which the epithelial layers are injured. If the attack is acute, and the superficial cells are detached or destroyed, absorption is rapid. Not only the poisons that are already present in the urine, but those produced by any septic or pyogenic organisms that may be growing in the bladder, pass into the circulation, and give rise to the gravest symptoms. That their action is not more often manifested is due to the fact that, under these conditions, a bladder keeps itself as empty as it can. Suppurative inflammation breaking out in a bladder that cannot empty itself causes the most intense form of septic poisoning.

On the other hand, in chronic cystitis, when the interior of the bladder is coated over with a mixture of pus and phosphate of lime, there is little or no absorption. Large doses of morphia may be injected into a bladder in this condition without producing the least effect, local or otherwise. But I have known a serious degree of absorption take place in cases in which there was ulceration of the mucous membrane in the presence of residual urine.

The behaviour of the urethra in this respect is entirely different. Absorption takes place readily whether the surface is inflamed or not. In those who are susceptible to its influence, I have many times known an injection of cocain followed by definite constitutional symptoms, within the space of a few minutes.

Glands. There are no glands in the bladder. The question of their existence has been discussed many times, and it must now be regarded as definitely answered in the negative. Little depressions in the form of pits may be found here and there (F. Hey, *Beit. zur Klin. Chirurgie,* Bd. 13, Heft 2, 1895), but no glands and no papillæ. Exceptionally one or two are present near the orifice, at the apex of the trigone; but these are stray ones that have been displaced from the mucous membrane lining the urethra in the course of development. According to Schäfer (Quain's *Anatomy,* vol. i., part i., p. 122) the ureters which are originally prolonged from and open into the Wolffian ducts, subsequently become shifted in position, so as eventually to open into the enlargement of the allantoic stalk from which the bladder is formed. The prostate, as I have shown (*Journal of Anat. and Phys.,* vol. xxix.) undergoes a similar change in the course of racial evolution, though it is not carried quite so far. Every now and then, however, some of the mucous glands that are normally present in the prostatic portion of the urethra, are detached from the rest, and carried on beyond into the neck of the bladder itself. With the exception of these there are no glands in the bladder.

The impression that acinous and tubular secreting glands are normally present in the bladder, especially in the region of the neck, has probably arisen from the irregularity in the base line of the epithelium. The division between the epithelial layers above and the connective tissue beneath is broken and interrupted in the bladder. Delicate little ridges grow upwards into the epithelium, without quite reaching the surface. These upgrowths, branching and joining laterally with neighbouring ones, mark out a kind of network, the meshes of which, filled with epithelial cells, are easily mistaken for the acini of a secreting gland. According to Aschoff (Virchow's *Archiv.*, 138, Heft 1, p. 119) this netlike arrangement, which is best seen in a horizontal or very oblique section near the surface, is as plain in the infant as it is in the adult. It is quite independent of the state of the bladder, whether it was full or contracted at the time when it was hardened, and is present equally upon the ridges and in the depressions between them. There is no doubt therefore that it is normal and not pathological.

The epithelial downgrowths described by von Brunn (*Archiv. f. Mikros. Anat.*, Bd. 41, 1893, p. 294) in the same region of the bladder, in many respects closely resemble tubular glands. They spring, not unfrequently, from the little blocks of cells that occupy the meshes of the network, and grow downwards, as solid columns, dividing and branching as they descend, like a racemose gland. But there is never any central cavity; the cells are not arranged as they are in secreting glands; they are not constantly present (Lubarsch, *Archiv. f. Mikroscop. Anat.*, Bd. 41, 1893, p. 303) and, as has been pointed out by Aschoff (*loc. cit.*), though they do resemble the true urethral glands in the mode of their development, they are not to be found in the bladder until adult life, at the earliest. Probably, therefore, they are to be regarded as pathological structures, caused by prolonged work or overstrain. Similar bodies have been described in other parts of the urinary passages, always above a place at which there is a natural constriction, and where, consequently, pressure is higher and more irregular than it is elsewhere.

There are no goblet-cells or mucus-secreting cells in the bladder. As there are no glands, it follows that the small quantity of mucus that is present in the urine comes from the urethra and its accessory structures, and not from the bladder itself.

Lymph Follicles. Structures resembling lymph follicles have also been described in the mucous membrane of the bladder (Chiari, *Wiener Med. Jahr.*, 1881, p. 9, and Ebstein, *Deutsch Archiv. f. Klin. Med.*, 31, 1882, p. 63). They make their appearance as minute, pale coloured points, projecting slightly above the surface, chiefly in the neighbourhood of the neck. According to Aschoff they are due to the growth of connective tissue septa upwards, into the epithelial layer. Delicate bridges of connective tissue, so fine that they can sometimes only be traced by the blood vessels they contain, extend upwards towards the surface and converging together enclose a number of the deeper lying epithelial cells in a kind of follicle, which may at length become completely closed. The cells in these follicles all point upwards towards the surface. The lower ones are cylindrical, the upper ones flatter; and according to the same authority, their shape and position are distinctive of their origin. Later, the follicles may enlarge into definite cysts, often lying in groups plainly visible to the naked eye. Like the epithelial downgrowths described by von Brunn, these follicles are found in other parts of the urinary passages as well as near the neck of the bladder. They are always placed immediately above some constriction, and probably are caused by some slight, but persistent source of irritation, such as increased and irregular pressure. There is no evidence that they are in any way connected with the lymphatic system ; and, in spite of the superficial resemblance they present, they are not lymphatic follicles.

The muscular coat of the bladder. This is arranged in three layers, an outer and an inner composed of longitudinal fibres, and a middle one of circular or transverse ones. The bundles are placed very irregularly, and except at the trigone, do not form a continuous layer, so that the interior of the bladder is often marked by diamond-shaped depressions. These, if there is any obstruction to the exit of the urine, sometimes grow so deep as to form pouches or sacculi, projecting on the exterior.

In the intervals between acts of micturition the muscular coat is in a state of tonic contraction, and keeps up a continuous though slight degree of pressure upon the contained urine. The amount of this pressure never remains exactly the same for any length of time. Peristaltic waves of alternate contraction and relaxation are continually coming down the ureters and spreading from them over the bladder. Stimuli starting from the mucous surface, or from other parts of the body are constantly acting upon it. According to Griffiths (*Journal of Anatomy and Physiology*, 1894-95, p. 254), physical efforts and mental emotions of all kinds influence it; and Ashdown (*Journal of Anatomy and Physiology*, vol. xx., p. 299) has shown that every slight change in the character or reaction of the urine affects it, the addition of a few drops of dilute hydrochloric acid, or of an alkali, for example, causing an immediate relaxation and fall in pressure.

It is this power of tonic contraction that enables the bladder to adapt itself with such ease and rapidity to the continual variations in the quantity of urine. So long as the distension does not overpass the limit within which the muscular fibres are able to work, the pressure in the bladder (putting aside for the moment that additional amount which arises from the weight of the fluid) is almost independent of the quantity of urine present. As the urine collects, the tension slowly rises, the rhythmic waves of contraction that are always spreading on to the bladder from the ureters, become slightly stronger, a sensation of uneasiness is felt, and a stimulus passes up from the neck of the bladder to the controlling centre in the spinal cord. If micturition is to follow, the voluntary sphincter at the apex of the prostatic portion relaxes, the pressure rises still higher under the influence of the central nervous system, and the bladder empties itself. At the end of the act, the tension falls once more to its former level.

If, on the other hand, micturition is not to take place, and matters have not already gone too far, the muscles that form the wall of the bladder relax a little, the carrying capacity is increased, the latest addition to the pressure is withdrawn again, the strength of the rhythmic waves diminishes, and the desire passes away. The bladder has adjusted the size of its cavity so that it can hold a larger quantity of urine, without materially altering the pressure upon it, in the same way that the blood-vessels can adapt themselves (within limits) to an increase or a diminution in the amount of circulating blood. But this only holds good for a time. The urine continues to flow in from the ureters, and sooner or later, according to the sensitiveness of the bladder and the amount of fluid present already, the tension limit is reached once more and the desire returns.

This may happen more than once, the bladder each time accommodating itself to the increased quantity. When the limit is reached, and the muscular fibres cannot adapt themselves to any further increase, the bladder behaves like any other elastic receptacle. The vesical pressure rises step by step with the quantity, until the resistance at the orifice gives way.

The sphincter of the bladder. There is no internal sphincter in the normal bladder. Guthrie (*Anatomy and Diseases of the Urinary Organs*) long since pointed out that the voluntary sphincter of the bladder is at the end of the prostatic portion of the urethra, not at the so-called neck. Fluid that enters the urethra anterior to the constrictor urethræ escapes by the penis; that which enters posteriorly, when it has filled the prostatic urethra, regurgitates into the bladder. I have examined the neck of the bladder in a very large number of specimens and have never been able to find, in those that were normal, any collection of fibres that deserves to be called a sphincter. Griffiths has found the same (*Journal of Anatomy and Physiology*, vol. xxv., p. 544). Probably much of the discrepancy of opinion that exists upon this subject has arisen from the different conditions of the bladders that have been examined. It is undoubtedly true, that as a result of continued irritation, the circular muscular coat at the neck may become enormously hypertrophied, but nothing deserving to be called a sphincter is to be found in this situation in the healthy bladder of a young adult of either sex.

At the same time it is perfectly true that no urine is allowed to enter the prostatic portion of the urethra until micturition begins. If the prostatic urethra is incised, urine does not escape. But if the incision is carried into the neck of the bladder, it flows away continuously. There is no sphincter at the neck of the bladder, but there is sufficient resistance to prevent urine escaping into the urethra.

Griffiths, who has performed a number of experiments upon dogs, with a view of ascertaining the nature of this resistance, concludes (*Journal of Anatomy and Physiology*, 1894-95, p. 254) that it is essentially physical in character, but dependent for its production upon the tone of the muscular structures around. The pelvic splanchnics and the hypogastric nerves upon both sides may be divided without weakening it. Even division of the spinal cord makes little or no difference to it. The real cause is the apposition of the mucous surfaces, and the unexpanded condition of the surrounding tissues; and these, in their turn, are the result of the tonic contraction of the muscles. The resistance does not cease with the death of the animal, but if, after death, it has once been compelled to give way, it is not reproduced. Fluid poured into the bladder under these conditions flows away at once,

The regulation of the orifice of the bladder and the nature of the stimulus that calls forth micturition. At the beginning of micturition the first portion of the urethra becomes funnel-shaped; the bladder and the urethra form one cavity; and the wave of contraction that passes over the former spreads on to the latter without a break, driving the contents into the part that lies below. This change in the shape and relation of the vesical outlet is due in part to the relaxation of the muscles that surround it, in part to the pressure of the urine driven into it from above. It is a passive and not an active process for there are no muscular fibres that are capable of dilating the orifice by contracting. The longitudinal bundles upon the outside of the bladder, which have been supposed by some to possess this power, are not inserted into the neck. They are either attached to the puboprostatic ligaments or they sweep obliquely round and are lost upon the outer surface of the prostate.

The stimulus that sets in action the master centre for micturition, starts, under ordinary circumstances, from the neck of the bladder. The rest of the interior of the bladder is comparatively insensitive. In exceptional instances the stimulus may originate from an irritation of other nerves, such, for example, as those distributed to the penis or the anus. As a rule it is attended by sensation, the so-called *bésoin d'uriner,* but this is not essential; micturition can take place equally well without it.

The stimulus is said to be due either to the contact of the urine with the mucous surface at the neck, or to the entrance of the urine into the prostatic portion of the urethra. But in a healthy bladder, one that has not been irritated in any way, neither the one nor the other of these is the real cause.

That it is not a mere question of contact is evident from the fact that the neck of the bladder is normally its lowest part, and therefore is always in contact with the urine. Moreover, the mucous surface of the bladder, so long as it is not inflamed is not especially sensitive to contact. Large calculi, if they are smooth and rounded in shape, may lie in the bladder for years without their existence being known ; and if instruments, such as lithotrites, are gently used, contact with the mucous surface, except at the instant that the neck of the bladder is opened, scarcely gives rise to any sensation. All this is changed when inflammation sets in ; then the mucous surface becomes intensely sensitive.

Nor is there more to be said in favour of the theory that under normal conditions the stimulus is supplied by the entrance of a few drops of urine into the prostatic portion of the urethra, although this has met with strong support from Kuss and Duval. In many cases of enlarged prostate, the first portion of the urethra is permanently dilated, and forms a cavity which, owing to the shape of the growth, is in open communication with the bladder and is constantly filled with urine. So long, however, as there is no irritation or congestion at the neck of the bladder, there is no increased frequency of micturition, or increased desire. And injections, even injections of nitrate of silver, may be made into the prostatic urethra without causing more than a momentary sensation. The entrance of urine into the prostatic urethra is the first part of the act of micturition (there is reason to think that the presence of urine in this portion of the urethra, exerts, for the moment, an inhibitory influence upon the tonic contraction of the muscle that surrounds the neck of the bladder); but it is the consequence of the contraction of the rest of the bladder, not the cause.

The tension of the walls is the real stimulus. While the bladder is filling the muscular coat is in a state of tonic contraction; the orifice remains closed, and no stimulus that excites sensation reaches the central nervous system. The mind is not conscious of the existence of the bladder. All this time, however, waves of alternate contraction and relaxation are spreading on the bladder from the ureters. So long as the bladder can accommodate itself to the increasing amount of urine, so that the tension does not rise, these waves are lost upon the wall. But as soon as this point is past, they increase in strength, as always when unstriped muscular fibre meets with unaccustomed resistance; the tonic contraction at the neck is either overridden or inhibited; the orifice relaxes, and if the voluntary sphincter is not brought into play, the urine is driven down into and through the prostatic portion of the urethra.

Guyon compares the bladder to the parturient uterus, the contraction of whose walls is the cause of labour pains.

How sensitive the bladder is to increased tension must have been noticed by every one who has ever performed lithotrity. The crushing of the calculus, in spite of the repeated contact of the instrument and of the fragments with the mucous surface, does not cause anything like the same degree of reaction as the comparatively simple proceeding of washing out the bladder.

The shape of the bladder is of importance. A very slight alteration in it may lead to the presence of what is known as "residual urine," one of the conditions that is especially favourable to the production of cystitis.

In the infant, according to Symington, the cavity of the bladder, as the urine flows out, is narrowed into a cleft that lies almost vertically in the body between anterior and posterior walls. Strictly speaking, it extends in a line from the umbilicus to the commencement of the urethra. In the adult the lower part of the bladder, when it is empty, is cup-shaped, with the urethra descending from the centre, or nearly the centre, of the under surface of the cup. Into this cup, as the urine escapes, the upper part of the bladder gradually sinks until the cavity is obliterated. When the bladder is full, the roof is convex. Then it becomes almost horizontal, and at last, when the cavity is empty, concave, resting in the concavity of the cup beneath. Throughout, so long as no pathological change takes place, the orifice is the lowest point, and there is no dependent pouch that cannot be emptied voluntarily.

As age advances the shape often becomes altered. In men the upward growth of the prostate is the most important cause. As the gland increases in size it raises the orifice of the bladder (owing to the triangular ligament of the urethra extension of the prostate downwards is impossible) and forms out of the part behind the trigone, a pouch that may at length attain a size almost as great as that of the bladder itself. In women a somewhat similar result may occur in consequence of troubles connected with the uterus; but owing to the anatomy of the urethra, it rarely leads to cystitis in them, unless they are confined to bed and are unable to sit up.

The effects of this change in shape are intensified by rigidity and loss of power of the muscular coat. In young subjects the walls of the bladder are flexible and elastic, and the muscular fibres, when they contract, empty the cavity thoroughly and with ease. As age advances, even when there is no conspicuous pathological cause, such as enlargement of the prostate or stricture, the walls grow hard and rigid. The power of the muscles diminishes, they easily grow tired and if there is the least difficulty in expelling the urine, the attempt is given up, and some of the fluid is allowed to remain behind.

Other and equally important changes in the shape of the bladder may be induced in different ways. If there is any persistent obstruction to the outflow of the urine, or any constant source of irritation, such as a calculus, the weakest part of the wall yields under the strain, stretches, and becomes pushed beyond the level of the rest. The pouches that are formed in this way, sometimes consist of all the coats of the bladder. More frequently they are formed only of the mucous membrane that has been pushed out in the unprotected space left between the muscular bands. Pouches formed in this way, having nothing but connective tissue on the outside to act as a support, and never being able to return to the bladder the urine that is driven into them, in course of time yield and enlarge, until at length they develop into great sacs, that project under the peritoneal coat, and communicate with the cavity by an opening scarcely larger than a crow-quill.

This change in shape is not of great importance, so far as cystitis is concerned, so long as the urine that occupies the spaces is expelled at each act of micturition. If micro-organisms do gain entrance and begin to grow, they are carried away before much harm is done. Complete evacuation of its contents at each act of micturition is the bladder's greatest safeguard. But, unhappily, complete evacuation is not by any means always the rule. Hernial protrusions consist of the mucous membrane only, and are never able to expel their contents. An enlarged prostate, in many cases, forms a valve which, when the bladder contracts, closes the opening long before the urine has had time to escape. In either case the result is the same. Urine collects in one portion of the bladder, and remains stagnant there, mixed with epithelial débris, and kept at the temperature of the body. If any germs gain entrance, they are not expelled, but are kept in the bladder under the best possible conditions for their growth, in a nutrient medium that suits them to perfection.

PREDISPOSING CAUSES OF INFLAMMATION OF THE BLADDER.

Certain conditions that favour the occurrence of cystitis are usually spoken of as predisposing causes. The term, though a convenient one, is not altogether free from objection, for agencies that excite a mild degree of inflammation are often at the same time the predisposing causes for a more severe attack. The presence of ammonia in the bladder for example, is at once a cause of inflammation, and a condition that favours in a very high degree the action of septic organisms.

These conditions are the same as those that favour the occurrence of inflammation in other parts of the body. Everything that interferes with the function of the bladder, or that tends to impair the vitality of its tissues is a predisposing cause for cystitis.

Injuries and diseases of the nerves and nerve centres that control the bladder, for example, are commonly attended by cystitis. Inflammation of the bladder is liable to break out at any moment in paraplegia, whether due to fracture of the spine or to other causes, and in a very large proportion of these cases, is the ultimate cause of death. And the same thing is true of myelitis, of injury to the nerves that supply the bladder, and of all other similar affections.

These affections are not, however, the cause of the cystitis (those very rare cases in which intensely acute inflammation of the bladder, often ending in sloughing, suddenly breaks out without any apparent reason, in the course of an attack of acute myelitis, may perhaps be excepted). I have known cases of paraplegia, in which the condition of the bladder was neglected, continue for months, without a trace of cystitis. The urine drained away from the urethra as fast as it came down from the kidneys. The bladder remained distended to the utmost of its capacity. But there was no inflammation, and the urine continued clear, until a catheter was passed. The paralysis is not the exciting or the direct cause of the cystitis; but it supplies conditions that are exceedingly favourable to it.

The bladder, when the nerve centre that controls it is cut off or paralysed, loses the power of emptying itself. Artificial means have to be adopted to prevent over-distension. The mucous membrane is absolutely insensitive. The muscular coat cannot contract. The natural working of the tissues is stopped; their nutrition and vitality suffer, and they are unable to set themselves free from, or get rid of irritants, which, if the bladder were healthy and the nerve centres intact, would have little or no effect upon them. It is possible, by the exercise of the greatest care, to prevent the occurrence of cystitis in a case of fractured spine; but the general conditions are so favourable that neglect of the slightest precaution is almost certain to be followed by it. Few cases are exempt from it for long.

Everything, again, that interferes with the circulation through the bladder or the prostatic portion of the urethra favours the occurrence of cystitis. Congestion of the mucous membrane lining the neck of the bladder is the commonest of all predisposing causes. It does not matter whether it is active or passive; whether it is due to some chemical irritant, such as cantharides or ammonia, or to a mechanical one, as calculus; whether it is the result of long continued straining, or is merely part of an increased flow of blood through the pelvic organs, such as occurs during the menstrual period and in pregnancy. The superficial epithelial cells, upon which the protection of the deeper layers depends, are thrown off, and the softer and younger ones beneath, which are much less capable of resistance, are exposed. The vascular pressure is increased to such an extent that many of the small vessels give way. The lymph that fills the interstices between the tissues circulates more slowly, and at last becomes almost stagnant. Nutrition is impaired. The tissues are unable to defend themselves, and the slightest irritant is strong enough to cause an attack.

This is one of the reasons why cystitis is so common in connection with enlargement of the prostate. The constant straining, acting upon the valveless and enormously enlarged prostatic plexus, inevitably leads to passive congestion. The mucous membrane lining the neck of the bladder becomes so swollen and hard that the bladder can scarcely empty itself. This, in its turn, makes the straining worse, and at length the condition becomes so bad that the most trivial exciting cause is sufficient.

Everything that interferes with the function of the bladder, or prevents it from emptying itself completely at each act of micturition, favours the occurrence of cystitis. Retention of urine by itself never causes inflammation, even if it lasts for years. In old men with enlargement of the prostate, it is by no means unusual to find that the bladder retains many ounces, and even pints of unsuspected urine. It is never expelled, but it remains perfectly clear and free from all trace of inflammation until a catheter is passed. In cases of stricture of the urethra I have several times known the bladder distended, for weeks together, until the apex was on a level with the umbilicus, without there having been a sign of cystitis. There is no inflammation because there has been no irritant. Retention alone is not enough.

At the same time retention of urine is one of the strongest predisposing causes for cystitis. Not only does it provide an abundant supply of one of the best nutrient media for septic organisms, under the best conditions for their growth, but at the same time it impairs the vitality of the mucous membrane by keeping it in a state of constant congestion. I have several times, when performing supra-pubic cystotomy in cases of extreme distension, seen the veins that run down the front wall of the bladder filled to their utmost. As soon as the opening is made, and the contents escape, they collapse and empty themselves. And it is not uncommon, especially when the cause of the retention is enlargement of the prostate, to find that the urine, when it is drawn off, is deeply and uniformly blood-stained ; the vessels in the mucous membrane have given way under the pressure and poured their contents into the bladder. But though it prepares the way for it, retention never, by itself, causes cystitis.

Guyon (*Ann. des Maladies des Org. Genito-Urin.*, 1890, p. 130) and Barlow (*Archiv f. Dermat. und Syph.*, 25, 1893, p. 355) have proved this by experiments on rabbits. If a rabbit's urethra is tied, the mucous membrane of the bladder becomes intensely congested, the smaller blood-vessels give way, and blood is poured out into the thickness of the wall, and through the epithelium, into the cavity of the bladder. But provided precautions are taken to prevent inflammation extending upwards from the seat of ligature, cystitis never follows. Retention of urine does not, and cannot cause inflammation of the bladder. There is nothing, however, that prepares the ground for it so well.

Exposure to cold is usually considered to be an exciting cause for cystitis, but there is no evidence that it can act in other than an indirect way. Like intense depression and great fatigue, cold lowers the vitality of the tissues, so that they become less capable of protecting themselves. Alone, acting by itself, it cannot cause inflammation of the bladder. There must be some exciting cause, in addition to the cold, though it may be so slight as to be scarcely perceptible. When the defence has broken down, the weakest irritant is sufficiently strong.

Melchior (*Cystite et Infection Urinaire*, 1895, p. 140) has shown, by a series of experiments upon rabbits, that neither the application of ice to the pubic region, nor the injection of hot and cold water into the bladder, is able to cause an attack of cystitis. If, however, a culture of the bacillus coli (which under ordinary circumstances has no effect upon a healthy, uninjured bladder) is injected as well, cystitis always follows.

There is no evidence that, putting upon one side tubercle and tuberculous cystitis, there is any such thing as a constitutional predisposition to inflammation of the bladder. It is true that many old men who pass catheters for themselves enjoy a high degree of immunity from it, in spite of the fact that they systematically neglect every precaution, while others suffer from it every time an instrument is introduced; but this is capable of other explanations. It does seem probable, however, that a certain degree of immunity from some of the forms of urinary fever may be acquired in course of time. But the consideration of this point is better postponed until the part played by micro-organisms in the production of inflammation of the bladder and urinary fever has been discussed.

THE CAUSES AND CLASSIFICATION OF INFLAMMATION OF THE BLADDER.

The immediate cause of inflammation of the bladder is always a local irritant. It may be a mechanical or a chemical irritant; or it may be a living organism. Without one or other to act as an exciting cause, there is no inflammation. Cold, congestion of the mucous membrane, retention of urine, and the other agencies I have named, are undoubtedly of importance. They lower the vitality of the tissues, and weaken their power of resistance, but they do not cause inflammation. This can only be caused by an irritant that acts upon the bladder itself.

Of these irritants those that are purely mechanical or chemical do not give rise to suppuration in the bladder, any more than they do in other parts of the body. A calculus, for example, is an irritant, especially when it is small and sharply pointed. The surface of the bladder is constantly being bruised and pricked, until perhaps it is made to bleed. The walls are kept in a state of congestion. All the blood-vessels are dilated. The mucous and sub-mucous coats are thickened and filled with lymph, and the epithelial cells that line it are thrown off before they attain their full growth or development. But so long as the calculus is the only irritant that is present, this is the limit. There is no suppuration.

The same thing is true of chemical irritants, such as cantharides and ammonia. They may cause strangury and hæmaturia. The urine may become filled with shreds of epithelium and lymph and even with blood from the walls of the bladder. But as Müller has shown (*Virchow's Archiv.*, Band 129, Heft 2, p. 173), so long as they are the only irritants, there is no pus.

When living organisms are the cause, it is entirely different—so different that it has been proposed by some to confine the term cystitis to those forms of inflammation of the bladder that are caused by living organisms and to refuse it to all others.

These organisms do not differ in any respect, except that of relative frequency, from those that are met with in suppurative inflammation of other organs. What they are, and how they gain entrance into the bladder, I shall deal with later. Some are the ordinary septic and pyogenic organisms. Others, like the tubercle bacillus, the bacillus of typhoid fever, and the gonococcus, have a specific pathogenic power of their own.

For convenience's sake, therefore, the varieties of cystitis may be described according to their causes as simple, suppurative, and specific. In most instances, however (especially in cases that last for any length of time) there are several of these agencies at work together. It very rarely happens that pyogenic organisms fail to make their appearance in the urine in cases of calculus. The tubercle bacillus is nearly always associated with the bacillus coli and with organisms that lead to ammoniacal decomposition of urea in the bladder. And some of the specific organisms that cause cystitis, such as the typhoid bacillus, are pyogenic at the same time. This division, therefore, though convenient for description, will not answer as a basis for a system of classification.

Nor have the other methods of classification that have been proposed, more to recommend them. Rovsing, for example (*Sur l'Etiologie, la Pathogénie, et le Traitement des Cystites*, Kopenhagen, 1889) finding that ammoniacal decomposition of urea was present in 24 cases out of 29 (the balance being of tuberculous origin) suggested the following :—

1. Catarrhal cystitis without suppuration, in which the decomposition of urea is caused by non-pyogenic organisms ; and

2. Suppurative cystitis of which there are two varieties,
    (α) Ammoniacal, caused by pyogenic organisms; and
    (β) Acid, caused by tubercle bacilli.

This, however, implies that every case of cystitis in which the urine is acid, must be of tuberculous origin; and Rovsing has subsequently modified it.

Barlow (*Archiv. fur Derm. und Syph.*, 25, 1893, p. 636) rejects Rovsing's classification on the ground that inflammation precedes the decomposition of the urea, instead of being caused by it, and proposes another, based partly upon the morphology of the organisms present.

1. Cystitis, due to chemical agents, such as cantharides.
2. Cystitis, due to bacilli, such as the tubercle bacillus, the bacillus coli, the urobacillus liquefaciens septicus and the coccobacillus of Rovsing.
3. Cystitis due to cocci, such as the gonococcus, and the different forms of staphylococcus, streptococcus and diplococcus.

Guyon abandons the attempt at establishing a systematic classification and merely describes characteristic clinical types. From a practical point of view this has much to recommend it. Our knowledge of the subject is not as yet sufficiently exact to do more.

It is better that the peculiarly misleading term "catarrhal cystitis" should be dropped. As I have already mentioned, there are no mucous glands or mucus-secreting cells in the bladder. The tenacious glairy deposit, often spoken of as mucus, that clings to the bottom of the vessel in ammoniacal urine, is merely pus that has been altered by the alkali. The very small quantity of mucin that does exist in urine, comes from the urethra and its accessory structures.

Melchior (*Cystite et Infection Urinaire,* Paris 1895, p. 342) while he does not deny the possibility of catarrhal cystitis, has never met with it. Guyon (*Leçons Cliniques sur les Affect. Chir. de la Vessie et de la Prostate,* 1888, p. 611) expressly states that there is no variety of cystitis that is not purulent, and Cohnheim (*Vorles. u. Allg. Path.*, 1880, p. 490) affirms that pus is always present in the urine in cases of cystitis, whether the inflammation is acute or chronic.

Hallé has suggested that the name, catarrhal cystitis, should be retained for cases that occupy an intermediate position between suppurative cystitis and what is known as bacteriuria, cases, that is to say, in which the urine contains a very large number of bacteria and a few pus corpuscles. But it seems better to drop it altogether than to give it a new and somewhat different distribution.

SIMPLE CYSTITIS.

Inflammation of the bladder due to chemical or mechanical irritants in the absence of living organisms. The mucous membrane lining the bladder, like that which covers and protects other organs, becomes inflamed when subjected to prolonged irritation. The irritants may be mechanical, calculi, for example, constantly bruising the mucous surface of the neck and abrading the epithelium, or small sharply pointed crystals of uric acid or of oxalate of lime; or they may be chemical, like cantharides; so long as no micro-organisms are present, there is no suppuration.

The pathological changes that occur in simple inflammation of the bladder are easily described, but are seldom seen, as such cases rarely present themselves for examination. They are always most marked in the region of the neck, partly because calculi come into contact with this part of the bladder in an especial degree, partly because it is the most vascular portion and the seat of the greatest physiological activity. The mucous membrane is swollen and thickened. The blood vessels are distended. Often, if the attack has been severe, there are minute ecchymoses where the smaller ones have given way, and here and there are patches that have lost their lustre: the superficial layers of epithelial cells have been detached, and the younger, softer ones beneath are exposed. Through the cystoscope there is little to be seen but intense congestion of the mucous membrane. The urine is blood-stained and full of detached epithelial cells, but does not contain any pus or any micro-organisms.

It must be admitted that this form of cystitis is rather of academic, than of any practical interest. It rarely lasts in its original form for more than a few hours. At the end of that time, if the urine is centrifugalised, organisms can nearly always be found in the deposit and cultivated from it, and pus corpuscles are always present too. Micro-organisms, when there is any mechanical or chemical irritant at work in the bladder, appear to find little difficulty in entering in themselves or in multiplying there. The attack either subsides at once or becomes purulent. For this reason I shall leave the symptoms to be described with those that are present in the milder forms of suppurative cystitis.

The evidence with regard to the existence of this form of cystitis is almost entirely experimental. It can easily be produced in rabbits by injecting ammonia into the bladder and ligaturing the urethra (Müller. *Virchow's Archiv.*, Band 129, Heft 2, p. 173). The mucous membrane at once becomes inflamed. The epithelium is detached in shreds and flakes. The urine becomes blood-stained and cloudy, but it does not contain any pus corpuscles. A certain number of leucocytes are present, but they come with the blood, and are only present in proportion to the red blood corpuscles. The cystitis, therefore, is simple and not suppurative.

Rovsing, on the other hand, is of opinion that this form of cystitis is of common occurrence in man. He has described a number of organisms that possess the power of decomposing urea in the bladder. They are not pyogenic, and do not cause suppuration; but they lead to the production of ammonia in the bladder, and this, acting upon the mucous membrane as an irritant, gives rise to what he has called catarrhal cystitis.

The experiments, however, upon which Rovsing relies, scarcely bear out his conclusions. The urine, which he collected in sterile glasses, with proper precautions, was boiled to ensure its being sterile itself. The organisms in question were then planted in it. Subsequently it was found to contain ammonia. But the proof that the ammonia was formed through the agency of the organisms that grew in the urine is not sufficient. Normal urine often contains traces of ammonia, and when urine is boiled, some of the urea, enough to vitiate the experiment, splits up and forms ammonia, without the addition of any reagent. There is no proof, therefore, that the ammonia found by Rovsing was the product of the organisms that he planted. It may have been there independently of them.

So far as the human bladder is concerned, it has not been proved that ammoniacal decomposition of the urea ever occurs, except as the result of the action of certain organisms, all of which are septic and pyogenic.

In the vast majority of cases the organism is either the urobacillus liquefaciens septicus (the proteus of Hauser) or the staphylococcus pyogenes. (The power that the bacterium coli possesses of decomposing urea is doubtful. In the cases of cystitis in which I have found it pure, the urine has always been acid, and sometimes very strongly acid). Whenever, therefore, ammonia makes its appearance in the bladder in any appreciable quantity, it is of necessity accompanied by suppurative cystitis. The conditions under which ammonia can cause simple cystitis, as it does experimentally in rabbits, are never present in the case of man.

Some little time since, however, I had under my care a gentleman in whom these conditions were nearly fulfilled. Two years before, the pelvis of the right kidney had become dilated, but not sufficiently to destroy the secreting power of the kidney altogether. Then a communication became established between the dilated pelvis and the neighbouring bowel. Septic organisms made their way in ; acute inflammation followed, and the urea was decomposed while still retained in the pelvis of the kidney. The urine, as it entered the bladder, was strongly ammoniacal, and intensely irritating. Micturition became more and more frequent, until it was nearly incessant day and night, and attended with severe pain.

But in spite of this, the bladder, which was thoroughly explored through an opening in the perineum, was but slightly affected. Perineal drainage, allowing the ammoniacal urine to escape as fast as it entered the bladder, prevented any further change, but of course had no effect upon the other symptoms or the reaction.

SUPPURATIVE CYSTITIS.

Inflammation of the bladder caused by pyogenic organisms. With the exception of the form of cystitis just described, which is rarely, if ever, met with in actual practice, inflammation of the bladder is always attended by suppuration. "Il n'est pas une seule variété de cystite qui ne soit purulente" (Guyon. *Leçons Cliniques*, 1888, p. 611). It is true that suppuration may not be present in the very early stages of tuberculous cystitis, but unless the disease rapidly gets well, it never fails to make its appearance before long. Pyogenic organisms are practically never absent from the urine when the bladder is inflamed.

Normal urine, obtained directly, or with suitable precautions, from the bladder or the pelvis of the kidneys does not contain germs of any kind. This fact was first established by Pasteur in the year 1860 (*Compt. Rend. de l'Academie des Sciènces*, p. 76) and it has since been confirmed by Lustgarten and Mannaberg (*Vierteljahr. f. Dermat. und Syph.*, Oct., 1887) and by Lister, Guyon, Albarran and many others. In a case of ruptured ureter in a young girl, who was under my care some years ago, the urine collected and remained in the peritoneal cavity for upwards of a week, without causing peritonitis.

On the other hand, in every case of cystitis (with the above mentioned exception) the urine contains pus and various forms of pyogenic cocci or bacteria. If organisms cannot be detected in the deposit by means of the microscope, they can always be cultivated by growing them upon suitable media.

Not only are organisms always present, but, as has been amply proved by the experiments of Hallé, Albarran, Schnitzler, Melchior and others abroad, if they are cultivated and the cultures are injected into the bladder under suitable conditions, cystitis invariably follows.

As the other irritants that affect the bladder do not cause suppuration; as these organisms are always present in cases in which there is suppuration; and as it has been proved that they always excite suppuration when injected into the bladder under suitable conditions, these organisms, or their products, must be regarded as the immediate cause.

At the same time it is undeniably true that, in the majority of instances, these organisms are incapable of causing cystitis by themselves. The conditions must be suitable or they are harmless. For them to have any power there must be some accessory agent present, such as congestion of the mucous membrane, or retention of urine. If they are injected through the urethra into the healthy bladder of a dog or of a rabbit, they disappear entirely in the course of twenty-four, or, at the utmost, forty-eight hours. If they enter the bladder from the kidney, or the ureter (so that there is no affection of the wall of the bladder itself, as there must be when an abscess bursts directly into it) they pass out harmlessly with the urine.

Certain organisms that possess the power of breaking up urea, and extremely virulent cultures of the bacillus coli are exceptions. These need no accessory or predisposing cause. They are sufficient of themselves. The urobacillus liquefaciens septicus, and the staphylococcus pyogenes are two of these. If they are injected into the bladder in sufficient quantity they lead to the formation of ammonia, and this, by the irritation it causes, supplies the assistance needed. And according to Barlow (*loc. cit.*) certain cultures of the bacillus coli (the virulence of which has been intensified by careful selection) possess the same power. In this case, as the formation of ammonia is slow and uncertain, the additional irritant is probably supplied by the toxic products of the growth of the bacillus. At least it has been shown that some of these products possess the power of causing necrosis of the intestinal epithelium, and therefore, possibly, of the bladder epithelium also. However this may be, these organisms are to be regarded as exceptions. They are capable of exciting suppurative inflammation of the bladder by themselves, without the presence or the assistance of an accessory. Ordinary pyogenic organisms are not.

Pathological Changes.

I do not consider that there is any necessity in a work of this kind to enter into a detailed account of the changes that are produced in the bladder by inflammation. They are described at sufficient length in the ordinary textbooks. There are, however, a few particulars, relating chiefly to the action of the microbes upon the tissues of the bladder, which should not be passed over without notice.

The effect produced by inflammation is most marked in the region of the trigone and especially around the orifices of the ureters and urethra. Cases in which a calculus is lodged in some outlying part of the bladder, or in which the wall of the bladder is pushed out into the form of a pouch are exceptions. The neck of the bladder is the lowest part in nearly every position of the body. It is by far the most vascular, the blood-vessels converging to it from all sides and forming a very close plexus immediately under the epithelium. It is the most sensitive portion, and it is the seat of the greatest physiological activity. In comparison the rest of the bladder plays a subordinate and almost passive part.

Except in those cases in which extension of an inflammatory focus from some neighbouring organ is the cause of the cystitis, septic inflammation always begins, and its effects are always most marked upon the mucous surface. Only when it is of unusual severity, or when the attack has lasted some considerable time, does the inflammatory process extend into the deeper layers. Inflammation may, however, involve not merely the sub-mucous and the muscular coats, but the sub-serous, and even the serous one as well; and it may lead to the formation of extensive adhesions between the bladder and the coils of small intestine that lie upon its upper surface, or to abscesses in the perivesical cellular tissue.

Acute cystitis. In the slighter cases the mucous membrane only is affected, but even in the slightest it is intensely congested. Seen through the cystoscope, its colour is a brilliant scarlet, with branching lines marking the course of the distended vessels; and it bleeds at the slightest touch. Post-mortem, the redness of course has disappeared; but the effects of the congestion can be seen in the swelling and thickening of the mucous membrane, and in the red and purple stains that mark the spots where small vessels have given way. Unless the attack has been a very transient one, the surface has lost its polish; when examined under water, it is ragged and velvety, and marked here and there by flakes of adherent lymph.

In the more severe cases, the characteristic appearance of the epithelium is entirely lost. The superficial layers of flatter cells disappear altogether. Those that occupy their places are smaller and more rounded, and fall away from each other more readily. The cell substance is less abundant. Sometimes more than one nucleus is visible. In between the cells are numbers of smaller ones, that cannot be distinguished from pus corpuscles; and collections of similar ones can be seen occupying the meshes of the connective tissue beneath, chiefly by the sides of the smaller vessels. In places, here and there, the whole thickness of the epithelium is detached, and the mucous membrane beneath is either exposed, or is partially concealed by flakes of lymph. Occasionally, as happened in one case of intensely septic cystitis that was under my care, portions slough bodily away, and are found hanging in the interior in shreds. In the worst cases there are minute abscesses in the sub-mucous coat, and among the muscular layers; the serous coat is covered over with lymph; and there may even be collections of pus in the perivesical cellular tissue.

In acute suppurative cystitis, micro-organisms, either bacteria, or cocci, or both, are invariably present. The urine is full of them, so that it sometimes seems to be an almost pure culture. They are present in abundance on and among the epithelial cells; and especially when the cystitis is due to streptococci, chains and masses of microbes may be seen occupying the interstices between the tissues throughout the whole thickness of the wall.

Chronic cystitis. The longer the inflammation lasts, the more permanent and the more extensive the tissue changes become. Pyogenic organisms, when not sufficiently numerous or energetic to cause active suppuration, lead in course of time to a condition of sclerosis and dense fibroid induration that is scarcely less destructive. And this effect is greatly intensified, when, as in so many cases of enlargement of the prostate, vascular degeneration and chronic congestion are present as well. In such instances, the whole thickness of the wall becomes involved, not the mucous surface only, and all the tissues of which it is composed are affected more or less.

The mucous surface is always discoloured. It may be simply stained by ecchymoses, or it may be uniformly slate-coloured, or even black. Except in those cases in which the bladder is dilated, it is thicker and denser than natural. Its elasticity is entirely lost. Instead of accommodating itself smoothly and evenly to the diminution in size when the bladder contracts, it is thrown into coarse uneven folds. These leave between them irregularly shaped spaces that cannot easily be emptied, even with a catheter. The surface may be smooth and uniform. More frequently it is rough and villous, or covered over with granulations that bleed at the least touch.

Sometimes, especially near the neck of the bladder, it is studded with small semi-translucent vesicles, which, at first sight, present some resemblance to lymphatic follicles. And, more especially when there is an additional irritant, such as a calculus, or ammoniacal decomposition of urea, it may be studded with ulcers, the surface of which is coated over with a dense and foul-smelling layer of phosphates and other urinary salts, mixed with septic organisms and decomposing pus.

The epithelial cells are for the most part ill-formed and misshapen. In some places they are heaped up in little masses. More frequently, especially on the crests of the ridges and folds, the superficial layers have disappeared, and only the deeper ones are recognisable. Bacteria and micrococci can always be found adherent to them, and in the urine; but in chronic cystitis they are not so numerous as in the acute form, and they are not found to so great an extent in the deeper layers, even of the epithelium.

The muscular coat may be thin and soft, or it may appear to be hypertrophied, bars and trabeculæ standing out on the mucous surface, leaving lozenge-shaped depressions between them. But the amount of genuine muscular hypertrophy is very variable. Where the work thrown upon the walls of the bladder has been excessive in the early days of the disease, the increase may affect the muscular fibres chiefly, and even entirely. When, however, the attack has lasted for some length of time, whether there has been obstruction at the outlet from the bladder or not, the hypertrophy is generally more apparent than real. The increased thickness is due rather to the formation of fibrous tissue than to the overgrowth of muscular fibres. True muscular hypertrophy is almost confined to the earlier stages.

Suppuration among the muscular fibres is rare, unless there has been an acute attack, such as may be caused at any time by ammoniacal decomposition of the urea. Very few micro-organisms can be seen in the interspaces in microscopic sections, but the sclerosis and fibroid degeneration of the walls that are met with everywhere may be taken as evidence of their past action.

The walls of the bladder may be immensely thickened and rigid, or they may be so thin and flaccid as to appear in imminent danger of rupture. The cavity may be of enormous size, or so small and contracted that it can only hold a few ounces. Its shape may be uniform, or pouches, sometimes as large as the bladder itself, may project from the outer surface. In all cases alike, whatever has been the condition of the muscular coat in the early days of the disease, there is degeneration of the active muscular elements. In their place there is, instead, passive, inert fibrous tissue, which contracts and hardens here, and yields and stretches there, until the appearance and structure of the bladder are entirely altered, and perfect restoration of function is almost impossible.

Membranous cystitis. This name has been given to certain forms of inflammation of the bladder in which membranous casts of the interior, with or without portions of the bladder wall attached, have either been found post-mortem, or have been passed or removed during life. These casts show no sign of organisation. They consist of nothing but epithelial cells, coagulated lymph, urinary salts, and myriads of organisms entangled together. In a case recently recorded, Loewenhardt (*Archiv. fur Dermat. und Syph.*, 29, 1894, p. 151) found that the membrane was almost a pure culture of a giant streptococcus, like the S. giganteus of Lustgarten, though the cystitis was apparently due to a bacterium which decomposed urea and liquefied gelatin. In other instances micrococci and diplococci have been found, but as no attempt at cultivation was made, identification is impossible.

In all the cases of which I can find a record, the urine has been ammoniacal. In some the casts have covered only a portion of the interior. But they may involve the whole, and extend up the ureters, or down the urethra, or through a wound into the vagina, wherever in short the urine comes into contact with a mucous surface. It is significant, as giving a clue to their mode of origin, that if there is a wound leading into the bladder, the false membrane is always thickest and best developed in its immediate neighbourhood.

In the majority of instances this cast is a simple exudation, and does not involve more than the remnant of the epithelium still left adherent to the bladder wall. More rarely portions of the mucous membrane are detached and thrown off with it. More rarely still, the whole thickness of the bladder wall has been known to slough and come away, leaving the cavity of the bladder in open communication with that of the abdomen. Owing to these differences two varieties of membranous cystitis have been described, one in which the cast consists only of the false membrane, the other in which it contains some of the tissues as well. It is very doubtful, however, if this distinction can be maintained. The difference is one of degree not of kind, and Guyon (*Leçons Cliniques*, 1888, p. 845) has recorded a case in which the two forms were present together. Part of the bladder was lined by a false membrane, showing no sign of organisation ; over the rest, the mucous membrane was detached, and the cellular submucous layer exposed.

Membranous cystitis rarely occurs unless there is either an unusually intense infection of the urine, or some additional cause interfering with the circulation through the bladder (such as the pressure of a displaced gravid uterus) or the two together. It has not been shown that there is any essential difference between it and the most severe form of acute cystitis, such, for instance, as occurs when in a case of retention due to enlarged prostate, ammoniacal decomposition of urea suddenly breaks out in a bladder already disorganised from long continued chronic cystitis. As I have already mentioned, patches of lymph may often be found under these circumstances adhering more or less firmly to those portions of the inner surface from which the epithelium has been detached; and occasionally, when there is a foreign body present, such as a septic catheter, the sloughing involves the mucous membrane as well. I have on more than one occasion seen it hanging down in putrid shreds.

Casts composed of false membrane only have been met with almost as frequently in men as in women. Most of the instances in which the whole thickness of the wall has sloughed, have been associated with retroversion of the gravid uterus. In all probability it is the outcome of intense septic inflammation combined with pressure, causing gangrene, either directly or by cutting off the blood supply at some more distant point. In the few cases in which it has occurred in the male sex it has always been the result of injury, and the slough has very rarely included more than the mucous layer, or involved more than a small portion of the interior. Recovery has been recorded in several cases, even in those in which portions of the serous layer have separated and come away.

THE CHANGES IN THE URINE IN SUPPURATIVE CYSTITIS.

When inflammation of the bladder is caused by chemical reagents, such as ammonia or cantharides, the epithelium is detached in flakes, many of the small blood vessels in the mucous membrane give way, and much foreign matter, in the shape of epithelial debris, lymph, and blood is added to the urine (Müller). According to the concentration of the irritant and the length of time that it is allowed to act, there may be only a faint cloud, or the urine may be turbid throughout and deeply blood-stained. The blood may follow the urine, the urine itself being almost clear, or the two may be evenly mixed together. But nearly always the last few drops are more deeply stained than the rest. If the irritant has affected the prostatic portion of the urethra as well as the bladder, the urine may be preceded by a few drops of blood, or by a clot moulded to the shape of that part of the canal.

In suppurative cystitis there are the same changes; but over and above these, the urine contains pus, secreted by the wall of the bladder; micro-organisms of various kinds, and the products to which these give rise—gases, such as carbonic acid and ammonia; fatty acids and their amido-compounds; indol, and above all, certain poisonous substances known collectively as toxins, concerning whose nature, quantity and action very little is certain. Probably they are proteid in composition; they may not all be poisonous; undoubtedly some among them are capable of causing active fermentation.

There is no need, in a work of this kind, to enter into any detailed account of the appearance or the reactions of the urine in cases of inflammation of the bladder. They have been described many times already. The presence of various kinds of micro-organisms, however, and of the pus, and the other substances that are dependent upon them, has scarcely yet received the attention that it deserves.

The presence of pus. When the reaction of the urine is acid, pus forms either a light, floating cloud, similar in appearance to that which is present in simple cystitis; or a dense greyish deposit that quickly settles down at the bottom of the vessel. The difference depends upon the amount of pus, and the relative density of the fluid with which it is mixed. The deposit may be uniform in colour throughout; or if the urine contains blood, or a large proportion of acid urates (which are precipitated as the temperature falls), it may be marked by horizontal streaks of red or brown. If the urine is poured slowly from one vessel to another, the sediment flows quietly away in a stream that does not mix with the clear fluid on either side of it. Sometimes it contains little curd-like masses made up of urinary salts and pus corpuscles held together by a few threads of fibrin.

Under the microscope the deposit appears to consist almost entirely of pus corpuscles, the nuclei of which are well defined, and of micro-organisms of various kinds. Here and there are a few blood corpuscles, little masses of urinary salts (chiefly urates and oxalates), and some shreds of vesical epithelium.

In ammoniacal urine, on the other hand, the appearance of the deposit is entirely different. The pus corpuscles are so swollen that they can no longer be recognised as such. The nuclei disappear; the outline of the corpuscles becomes indistinct, and in a little while they fuse together into a viscid semi-translucent mass, which entangles in its substance all the micro-organisms, urinary salts and epithelial debris, and sinks to the bottom of the vessel. It is this mass that is often spoken of as mucus, or as a muco-purulent deposit. When the vessel in which it is contained is inverted, it clings to the bottom and sides, like a mass of tenacious mucus. But it consists merely of pus that has been altered by the alkali, and has no mucin in its composition.

In the worst cases, those especially in which the urine is putrid as well as ammoniacal in odour, there are filaments and shreds of false membrane. These show no sign of organisation. They consist only of pus corpuscles, micro-organisms, and urinary salts, (chiefly the ammonio-magnesian phosphate) held together by a fibrinous exudation that is poured out from the surface of the mucous membrane after the epithelium has been detached. Blood corpuscles are naturally of frequent occurrence in association with pus, whether the urine is acid or alkaline, but they soon disappear if the urine is allowed to stand.

Valuable information as to the portion of the urinary tract that is involved, may often be derived from the manner in which the pus presents itself. It may come from the urethra, or from the kidneys, or from suppuration in connection with neighbouring organs, as well as from the bladder.

Urethral pus is never evenly mixed with the urine. When micturition takes place, the pus is washed out with the first few drops, either as a turbid fluid or as a more or less coherent thread. The rest of the urine is clear.

There is more difficulty when the source of the pus is the pelvis of the kidney. If, however, the amount in the urine is large; if it fluctuates widely; or if the urine is acid and habitually of low specific gravity, it may be taken as certain that a great deal, if not the whole is of renal origin. The cystoscope here is the best guide. The condition of the mucous membrane of the bladder can be seen, whether it is inflamed or not, and occasionally a jet of turbid urine can be distinguished coming down from one of the ureters. In many instances, however, the final decision rests upon evidence derived from other sources.

Pus often finds its way into the urine from other neighbouring organs. This is especially the case with women. As a rule there is little danger of making a mistake. The examination of the deposit under the microscope, the history of the case, and the other symptoms that are present, point definitely to troubles elsewhere. But there may be considerable difficulty when, as not unfrequently happens, inflammation of the bladder is present in addition to, and perhaps in consequence of other disorders.

Micro-organisms are invariably present in the urine when it contains pus. It makes no difference whether the pus comes from the wall of the bladder, as in suppurative cystitis, or from the kidney, or as in a case recorded by Guyon (*Ann. des Mal. des Organes Genit. Urin.*, tome xi., p. 360) from an abscess that had formed a communication with some of the urinary organs. Micro-organisms are never absent; they can always be recognised by the microscope or by making cultivations.

Bacteriuria. In certain exceptional cases of what has been called bacteriuria, micro-organisms are present either without pus at all, or with so little that the amount may be neglected. Sometimes they are present in such numbers as to make the fluid almost opaque. If the urine is centrifugalised they form the whole deposit. It consists of bacteria, urinary salts and nothing else.

It has long been known that the germs of certain specific diseases can pass through the kidneys and make their appearance in the urine without any pus corpuscles being present. The tubercle bacillus, for instance, has been found in the urine without pus, in cases of miliary tuberculosis, as well as in diseases of the urinary organs (Fardel, *Archives de Physiologie*, 1886). Philipowicz (*Wiener Med. Blätter*, 1885, No. 22), discovered the bacilli of anthrax and of glanders in the urine of animals suffering from those diseases, and was able to cultivate streptococci from the urine of two cases of ulcerative endocarditis and erysipelas. Schweiger (Virchow's *Archiv.*, Band 100, Heft 2) has shown that the urine of patients suffering from scarlatina and varicella may be contagious. And quite a number of cases are on record in which the bacterium of typhoid has been found in the urine.

Nor is this true of specific organisms only. Pyogenic cocci are sometimes present in the urine without any pus. In such diseases as acute osteomyelitis and ulcerative endocarditis this might be expected; but it is said that they have been found in the urine in cases in which there was a simple local abscess, and even in some in which there was no suppuration at all. Enriquez (*Semaine Medicale*, 1891, No. 57, p. 468) found the staphylococcus pyogenes in the blood, and in the urine of four patients out of sixteen who were living in the same ward.

In these cases micro-organisms of various kinds were present in the urine by themselves. There was no pus. But they are not to be regarded on that account as cases of bacteriuria. The number of organisms present was small. They had not grown in the urine; they had merely been excreted with it. In genuine bacteriuria the germs are present in such numbers as of themselves to render the urine turbid and form the main bulk of the deposit.

Bacteriuria was first described by Sir W. Roberts (*Brit. Med. Journal*, 1881, vol. ii., p. 359). There is no inflammation of the bladder. The infection is that of the urine, not that of the mucous membrane. There are no pus corpuscles, but merely enormous numbers of bacteria growing in the urine while it is still retained in the bladder, in a manner analogous to that of the sarcinæ that are found occasionally in the same situation. The urine itself is greyish and opalescent; the deposit is very difficult to separate off, even with the centrifugal machine. If left to stand, it grows denser instead of clearing up, and there is a peculiar and most offensive odour of stale fish. It is the odour, as a rule, of which the patient complains more than anything else.

The bacterium present in Sir W. Roberts' cases is said to have been the bacterium termo, but it is noted that the urine did not readily become putrid. In the majority of instances the organism is the bacillus coli; but the bacillus prodigiosus has been found (Posner, *Berl. Klinik*, 1891), and a bacterium causing ammoniacal decomposition of urea. This case rests on the authority of Hallé. The patient was an adult, without any urinary history. The urine was fœtid, very thick, with a grey deposit of epithelium, carbonates, amorphous phosphates, crystals of triple phosphate and bacteria in myriads: but there was no pus. The patient was cured within a week by the internal administration of borate and benzoate of soda.

Other cases have been recorded by Ultzmann (*Vorlesungen über die Krankheiten der Harnorgane*, Wien, 1888, Heft 1); Stenbeck (*Zeitschrift für Klin. Med.*, 1892, p. 457); Melchior (*Cystite et Infection Urinaire*, Paris, 1895, p. 112); Krogius (*Ann. des Maladies des Org. Gen. Urin.*, 1894, p. 196), and Rovsing (*Ann. des M. des Org. Genito-Urin.*, 1897, p. 910). In very few of these was there no previous urinary history. In Ultzmann's there had been an abscess in the prostate. Of the eight cases recorded by Krogius, in the three men there had been more or less recent gonorrhœa, and in three of the five women recent inflammation of some of the pelvic organs; and of the ten cases of pure bacteriuria described by Rovsing, four were suffering from hæmaturia; four from enlargement of the prostate, necessitating the use of catheters; one from stricture, and one from incontinence of urine and tabes dorsalis. In all alike there was a complete absence of the symptoms that accompany inflammation of the bladder. There was no increased frequency of micturition or pain; and in the three in which a post-mortem examination was made, the mucous membrane of the bladder and the pelvis of the kidneys showed no sign of having been inflamed.

In Sir W. Roberts' cases there were no constitutional symptoms. Some of them had continued off and on for years, the bacteria appearing for a time and then vanishing again, without causing any ill-effect. But this is not always so. In one instance, recorded by Runeberg, that of a young man, 22 years of age, who was suddenly seized with bacteriuria after having suffered from gleet for some years, the effect was exceedingly serious. There were no local symptoms; no pain or increased frequency of micturition; and nothing but the appearance and the odour of the urine to call attention to it. Suddenly, without warning of any kind, he was attacked with rigors, vomiting, and high fever; and these symptoms returned every two or three days for upwards of two months. The spleen became enlarged and the patient's strength was rapidly becoming exhausted. Constitutional treatment was of no avail. The symptoms quickly subsided after the bladder had been washed out with a solution of nitrate of silver.

Krogius (*loc. cit.*) mentions several others in which symptoms of a similar character were present. The urine in them all was acid and contained myriads of the bacillus coli.

These cases bear out the experiments performed by Boyer and Guinard (*Société de Biologie*, June 18th, 1894). The toxins produced by the bacteria while in the bladder are not absorbed so long as the epithelium continues to be healthy and uninjured. But if the toxins become concentrated, or the epithelial cells are kept in continued contact with noxious substances, their vitality is impaired and absorption takes place as rapidly from the bladder as from almost any other mucous surface.

In the majority of these cases there is no difficulty in understanding how the organisms gained access to the bladder. In nearly all there was a history of previous instrumentation, or of recent inflammation and suppuration in the urethra, or in one of the neighbouring organs.

In a few, however, the explanation is more difficult: and for these it may perhaps be necessary to adopt the suggestion made by Rovsing (*loc. cit.*), that the germs found their way into the bladder through the medium of the circulation, either directly, as in the cases of hæmaturia that he has described, or indirectly through the kidneys in cases of nephritis and pyelitis.

It is not so easy to account for the retention of these organisms in the bladder, and their multiplication there, for months and even years together, without their exciting any of the symptoms or appearances of inflammation. And the difficulty is not rendered less by the fact that in a certain proportion of cases, accessory causes, such as partial retention, were present at the same time. According to Rovsing it proves that the bacillus coli, though it may cause pyelitis, is innocuous so far as the bladder is concerned. The bacillus coli, however, it is well known differs very greatly in virulence according to the source whence it is derived and the circumstances under which it is grown. Moreover it must be remembered that even if the clinical signs of cystitis were not present in these cases, there were a few pus corpuscles to be found in the deposit in almost all. It is by no means uncommon for patients, especially in the later years of life to complain of the peculiarly unpleasant odour of their urine. If it is examined the bacillus coli is, so far as my experience goes, invariably present, and not unfrequently it forms the major portion of the deposit; but I have not yet found a case in which careful search has not shown abundance of pus corpuscles.

The presence of bacteria in unusual numbers may be suspected when the supernatant fluid continues to be milky after having been centrifugalised for the ordinary length of time. It should become perfectly clear.

In ordinary cases of suppurative cystitis the fluid that is left after the deposit has been separated off, contains traces of albumen, derived from the liquor puris; a globulin, formed by the disintegration and solution of some of the pus corpuscles ; various salts, derived partly from the urine, partly from the pus ; and the soluble products of the growth of the micro-organisms that are present. According to Guyon, it always contains a substance known as pyin, which is coagulated by heat, and precipitated in the cold by the addition of acetic acid. This reaction is accepted by him as evidence of the presence of pus.

THE ORGANISMS FOUND IN THE URINE IN SUPPURATIVE CYSTITIS.

To ensure accuracy, the urine must be collected directly from the bladder into a sterilised vessel, without being allowed to come into contact with the mucous membrane of the urethra; and the deposit must be thrown down and examined at once. If the urine is allowed to pass down the urethra in the ordinary way it becomes mixed with the secretions from the walls and from other organs, and contaminated by the addition of some of the organisms that, especially in the case of women, live in such profusion in or near the urethra. If the deposit is not thrown down and separated at once, it undergoes changes which modify, if they do not vitiate, the result.

Method. The precautions that should be taken have gradually been perfected, as the results obtained by one observer have been checked and improved upon by others. All instruments and appliances must be sterilised, preferably by heat. The hands, the glans penis (especially the meatus) and the prepuce must be thoroughly cleansed with soap and water, disinfected, either with corrosive sublimate, or, as preferred by Barlow, with a five per cent. solution of nitrate of silver, and then washed again and again with sterilised water, until all trace of the disinfectant has been removed. The urethra itself must be washed out from behind forwards with a saturated solution of boric acid.

Even then, if the urine is passed in the natural manner, cultures can nearly always be obtained from it. It is not possible to disinfect the mucous membrane of the urethra with certainty by simply washing it out (Melchior). Rejecting the first urine that is passed, and collecting only the last few drachms, is a useful precaution, but as Lustgarten and Mannaberg (*loc. cit.*) long since showed, almost as many cultures can be obtained from the last part of the stream as from the first. The urine, as it sweeps down the urethra, does not seem to make an appreciable difference in the number of organisms. In women thorough disinfection is almost impossible.

Barlow made use of an elastic catheter sterilised with steam and lubricated with sterilised glycerine. But the only instrument that can be relied upon is the catheter devised by Melchior. This consists of two tubes, one gliding inside the other. The outer is of metal and is sufficiently long to reach the bladder. Its vesical end is closed with a film of rubber, held in place by means of a metal cap. The inner one is flexible, about the size of a No. 6 English. Instead of this I always employ one of the aseptic catheters made for me by Messrs. Maw, Son & Thompson. The inner surface of these is as highly finished as the outer ; there are no irregularities to harbour germs, and they can be thoroughly sterilised by boiling without injury. As soon as the outer tube is in position, the inner is passed down inside it, and pushed through the rubber film directly into the vesical urine. In this way the catheter never comes into contact with the meatus or the mucous membrane and the urine obtained is as free from contamination as it is possible for it to be.

If the bladder is healthy, the hands and the external genitals thoroughly cleansed and disinfected, the instruments sterilised, and the urethra well washed out before the catheter is passed, sterile urine is generally obtained with Melchior's instruments. There are exceptions, but the cause of these I shall deal with later, when I come to discuss the various ways in which micro-organisms gain access to the urine.

It is always advisable to reject the first portion of the urine that is passed. That which follows comes from the lowest part of the bladder, where the deposit is most abundant, and is a little more likely to be free from added germs.

The urine should, if possible, be collected directly into the tubes belonging to the centrifugal machine. The risk of contamination is greatly increased if it has to be transferred from one to the other. Even when it appears to be perfectly clear, a certain amount of deposit, sufficient for microscopic purposes and for cultures, can nearly always be obtained by a few minutes revolution. Gärtner's instrument is exceedingly simple and rapid, three minutes usually sufficing; but there are several other hand machines, such as Daland's, equally good. Those driven by water-power or an electric motor are more suitable for laboratories. Part of the deposit is to be used for microscopic examination, the rest for the preparation of cultures.

As regards the former of these I need not enter into any detail. The microscopic examination of urinary sediments does not require to be described here. It is essential, however, that in addition to the ordinary methods employed, cover-glass preparations should be made for the purpose of identifying the various kinds of organisms, and comparing them with those obtained from cultures. Methylene blue, fuchsin or gentian violet may be used to stain them; or they may be treated by Gram's method, and then, as they have to be kept a few days, until the cultures have grown up, mounted permanently.

The only satisfactory way of separating out the different varieties of organisms that are present is to make use of plate cultures on gelatin or agar. Secondary cultures on serum, gelatin, milk, or potato, can then be taken from them.

As a matter of actual practice this is scarcely necessary in dealing with the urine from a case of suppurative cystitis. I adopted it in the first ten of my cases; but such an enormous preponderance of one or two kinds of organisms was found in each, that in the remainder only such an examination was carried out as would suffice for clinical purposes. My object was not so much to find out how many different kinds of organisms were represented, as to ascertain in the easiest and simplest way—a way that can be adopted by a busy practitioner, what were the predominant ones at the time. A sufficiently accurate idea can be formed if sterilised tubes of gelatin, serum, sugared bouillon, and milk, and the cut surface of a boiled potato are inoculated from the deposit with a platinum needle. An incubator is, of course, a great advantage. But although it takes a little longer to develop them, fairly satisfactory results can be obtained at the ordinary room-temperature. All the organisms that are commonly met with in urine grow readily without artificial heat.

As I have already mentioned, normal urine obtained directly from a healthy bladder with suitable precautions, is sterile. In suppurative cystitis it always contains organisms.

Excluding cases of tuberculous disease, I have examined the urine from thirty cases of suppurative cystitis. In twenty-four the reaction was acid or neutral, and in six alkaline. Organisms were present in abundance in all.

The bacterium coli was present in twenty-one of the acid urines and in four of the alkaline ones; and in fourteen out of the twenty-one it was present in such preponderance as to form an almost pure culture.

The streptococcus pyogenes was the next most common, but its frequency was much less. I found it in four only of the acid urines (in one almost pure) and in three of the alkaline ones.

A bacillus that appeared to be identical with the urobacillus liquefaciens septicus of Krogius (including its power of decomposing urea) was present in five out of the six alkaline ones.

In addition to these I found a staphylococcus present in eight; a diplococcus (which perhaps was only a form of the bacillus coli) in two; and in one a bacillus I could not identify with certainty.

As a thorough system of plate cultivation was adopted in only one-third of these cases, the results must be regarded as approximate only. Organisms may easily have been overlooked, especially when two or three varieties were present at the same time. Still, they agree fairly well with the greater number of those rècorded by other observers. Thus Hallé and Albarran (*Bulletin de l'Académie de Médecine*, Aug. 21st, 1888) found a bacterium, which has since been identified as the bacillus coli, in 47 cases of cystitis out of 50, and in 15 of them it was practically a pure culture. Morelle found it in 13 out of 17, associated twice with the staphylococcus pyogenes aureus, and five times with the streptococcus pyogenes. Krogius found it in 16 out of 20; and Melchior in 24 out of 35, of which five should be excluded as being due to the action of specific organisms, the tubercle bacillus, the gonococcus, and the bacillus of typhoid fever respectively.

The different results that have been obtained by other observers may probably be accounted for by the fact that the cases were chosen from a limited class. Bumm, for example, (*Zur Ætiol. der Puerperal Cystitis. Verhand. der deutsch Gesell. für Gynæk.*, 1886), found diplococci, some resembling gonococci, others like staphylococci, in eight cases of puerperal cystitis. Schnitzler (*Zur Ætiol. der Cystitis*, Wien, 1892) examining chiefly cases of cystitis in women who had been operated upon for cancer of the uterus, found a micro-organism capable of decomposing urea in 23 out of 25; while in the cases described by Rovsing, ammoniacal decomposition was present in 24 out of 29, the five exceptions in which the urine was acid being of tubercular origin.

The majority of my own cases were men who were suffering from enlargement of the prostate. Three only were women.

The bacillus coli may therefore be regarded as the organism that is most frequently present in the urine of suppurative cystitis when it is acid; and the urobacillus liquefaciens septicus (the proteus of Hauser) when it is ammoniacal. The latter, however, rarely exists as a pure cultivation, like the former. The staphylococcus pyogenes and the streptococcus occur in a considerable proportion of cases, rarely by themselves, almost always associated with one or both of the preceding forms. Excluding specific organisms, such as the typhoid bacillus, the gonococcus, and the tubercle bacillus, the other organisms that have been found may be accounted for either as the outcome of special conditions, like the diplococcus described by Bumm, or as isolated and rare examples.

The bacillus coli is a short bacillus with rounded ends, capable of moving, but not so actively as the proteus. Its length depends greatly upon the conditions under which it is grown. In old cultures or those in which the soil is not very suitable, it may be so short as to be mistaken for a coccus, and it has been described as a cocco-bacillus. Grown upon young potato its length may be many times its breadth. Occasionally certain portions of the organism absorb colouring material much better than others, so that unstained portions appear here and there; but there are never any spores.

It does not liquefy gelatin. If planted beneath the surface, it forms little rounded masses, translucent at first, and yellowish by transmitted light. Later, they become darker and more opaque. On the surface the young colonies are transparent; the older ones are opaque in the centre, with transparent rings around them. In stab-cultures, the whole length of the puncture grows, so that with the surface growth, it presents somewhat the appearance of a flat-headed nail. Bubbles of gas are often developed beneath the surface. After a time the cultivation becomes granular in appearance, and little outgrowths spread from it into the surrounding mass.

On agar and serum, the bacillus coli forms a white opaque patch with irregular edges. It coagulates milk rapidly, and if any dextrose or lactose is present it sets up fermentation, and causes bubbles of gas to collect beneath the surface. On potato it grows readily, especially when the surface is slightly acid, forming a slimy yellowish coat, which later becomes dark brown. Whereever it grows it gives off a faint and most unpleasant odour.

Whether the bacillus coli is capable of effecting the decomposition of urea or not, is still a little uncertain. Melchior agrees with Barlow, Achard and Renault, (*Soc. de Biologie*, Dec. 3rd, 1892), Morelle, and others, in denying its power. It is noteworthy, however, that in two of the cultures that he records, ammoniacal decomposition did occur at last, (*Cystite et Infection Urinaire*, Paris, 1896, p. 130). On the other hand Krogius (*Rech. Bact. sur l'Infection Urinaire*, Helsingfors, 1892), and Albarran and Hallé, (*Acad. de Médecine*, 1888), assert that it can.

With the view of determining this question Hallé and Dissard (*Ann. des Mal. des Organes Genito-Urinaires*, May, 1893), carried out a very thorough series of experiments. The urine was sterilised by means of a Chamberland's filter, and tested by being kept in an incubator for from four to eight days before being planted. The growth was taken from many different sources. The amount of urea was estimated after the carbonate of ammonia and proteid derivatives that are ordinarily present in the urine had been eliminated, and control experiments were made at the same time. The conclusions at which they arrived, were, that actual fermentation of urea did take place under these circumstances. The production of carbonate of ammonia was proportionate to the disappearance of the urea; but the process was carried out very slowly and never completely. A certain amount of unchanged urea was always left, even when the experiment was kept up for twelve months. They also found that this power was possessed by different specimens of the bacillus coli in very different degrees; and that in none was it to be compared with that of the proteus or of the staphylococcus pyogenes.

As the bacillus is so frequently present in cases of suppurative cystitis in conjunction with highly acid urine, it is not probable that, even if it possesses the power, it exercises it to any extent while in the bladder.

Many of the substances found in cultivations of the bacillus coli are of great importance. Some of them are well known. The existence of others is only inferred from their physiological action.

Indol, for example, is always present, and is, in part at least, the cause of the peculiarly offensive odour given off by cultures of this bacillus. It may be recognised by the red colour that it forms on the addition of potassium nitrite and sulphuric acid.

A ptomaine, known as putrescin, has been found in old cultures by Gautier (*Les Toxines*, p. 80). In itself putrescin does not appear to be poisonous. It is, however, very easily decomposed; and the products of its decomposition, if injected into the body, produce the same effect as neurin and muscarin. In the intestine it is said to cause necrosis of the epithelial lining.

According to Buchner (*Centrlb. f. Bacteriologie*, 8, 321) the substance of the cell-wall is strongly pyogenic. Living or dead, the bodies of the bacteria are capable of causing suppuration, independently of any soluble ferment.

The soluble products of the growth of this bacillus have been investigated by Gilbert and Hallé. The former (*Semaine Médicale*, 1893, p. 97), made use of a culture in bouillon, obtained directly from the stools of a healthy adult. The latter (Melchior, *loc. cit.* p. 145, note) grew the organism in urine. The bacteria were separated off by means of a Chamberland's filter, and the soluble products injected into the auricular vein of a rabbit. The results were almost identical. A large dose caused muscular tremors and convulsions, followed by paralysis and coma, with nystagmus, exophthalmos, tetanic spasms and death. A smaller one was followed by diarrhœa, loss of temperature, polyuria, somnolence and emaciation, the animal often dying at the end of a few weeks.

The nature of the toxins that are produced appears, therefore, to be the same, whatever the medium in which the organism is grown. Their virulence, however, is influenced by many different conditions.

The source whence the bacillus is derived, is described as having a peculiarly powerful effect. According to Lesage and Macaigne (*Archiv. de Med. Experiment. et d'Anat. Path.*, 1892), a growth cultivated from the contents of a healthy intestine is much less virulent than one taken from a case of infantile diarrhœa; and this in its turn, scarcely admits of comparison with one cultivated from choleraic discharges. Melchior has found an almost equal degree of difference in cultures taken from different cases of cystitis, and grown under precisely similar conditions. This is borne out by the experiments of others but it is manifest that there must be many other circumstances taken into consideration in deciding such a question as degrees of virulence.

The pathological effects produced by the injection of the bacillus itself are more variable. According to the amount injected and the circumstances in which the experiment is made, it may produce no effect at all; lead to inflammation and suppuration; cause death from toxæmia, either at once, or later from the cachexia it induces; or give rise to an acute form of septicæmia.

Injected into the subcutaneous tissue the usual result is an abscess. The amount must be proportionately very large to produce toxæmia. According to Sternberg guinea-pigs are more susceptible than mice. In dogs and cats it is scarcely possible to induce toxæmia in this way.

Intra-peritoneal injections in the case of rabbits either produce merely a temporary indisposition, or are followed by sero-fibrinous or purulent peritonitis (Melchior). In mice they are exceedingly fatal. If the amount is large, death ensues rapidly from toxæmia. According to Flügge (*Bacteriologie*, 1896, vol. ii., p. 366), enteritis with a subnormal temperature is the rule in rabbits, guinea-pigs, and mice, without distinction. If the amount injected is smaller, or the culture less active, death follows in the course of a few hours from septicæmia, the organism being found in abundance all over the peritoneal cavity, and in small clumps and masses in the blood-vessels. The earlier the death of the animal, the more abundant the growth in the peritoneal cavity. If the animal survives the septicæmia, it often dies later from the effects of the poison.

Injected directly into the blood, it acts with greater vigour still. Rabbits are killed in a very short time with symptoms of general toxæmia, collapse, diarrhœa, convulsions, dyspnœa, and a temperature usually below normal. The effect in other words is the same as when the toxins are used by themselves. Smaller amounts may either prove fatal in a few days from septicæmia, or the animal may recover. Very often, however, the recovery is incomplete and death ensues later, in the course of a week or two with symptoms of general exhaustion.

As might be expected from the fact that many different observers have been working under different conditions, there is a certain amount of discrepancy in the results obtained; but this only applies to minor and quite insignificant details. There is a sufficient degree of uniformity to justify the conclusion that the bacterium coli (or an organism that belongs to that group) which is ordinarily a harmless saprophyte in the intestine, has the power, if it is injected into the tissues, of causing local suppuration, toxæmia, or general septicæmia, according to the circumstances under which the trial is made.

At the same time, unless the conditions are exceptionally favourable, the bacillus coli does not readily give rise to septicæmia. The bacillus must be injected into the peritoneal cavity, or into the blood itself; and the amount injected must be considerable in proportion to the size of the animal. Subcutaneous injections either prove fatal from toxæmia, or end in local suppuration.

Mixed injections, in which, for example, the streptococcus pyogenes or the staphyloccus is present, as well as the bacillus coli, appear to be followed by general infection with greater frequency. Wyssokowitsch has shown that the virulence of bacteria which do not in general grow in the tissues, may be increased by the simultaneous injection of the toxic products of other bacteria, the bacillus coli in particular. And it is not improbable that, as Watson Cheyne has shown in reference to other organisms, the simultaneous injection of a comparatively large amount of its own toxic products, may enable the bacillus coli to gain a stronger foothold in the tissues than it otherwise would, and cause septicæmia.

The urobacillus liquefaciens septicus, the other bacillus that is commonly found in the urine in cases of suppurative cystitis, is identical with the proteus of Hauser. It is a short bacillus, with rounded ends, but its length depends greatly upon the conditions under which it is grown. All the ordinary aniline dyes stain it, and the colour is quickly removed by iodine.

It is much more active in its movements than the bacillus coli. When grown on a five per cent. solution of gelatin, whole colonies can sometimes be seen moving away from the central group. It liquefies gelatin rapidly at the temperature of the room. The surface of a plate culture becomes marked by a number of rounded depressions, white and opaque in the centre, each corresponding to the growth of a separate colony. As the colonies spread, the depressions increase in size until at last they meet and fuse together, so that the whole surface becomes covered with a liquid layer.

On agar it forms a thin transparent coat. It makes cane and grape sugar ferment, coagulates milk, and converts albumin into peptone, with the evolution of an unpleasant odour and the production of a substance identical with the sepsin of Bergmann. Urea is decomposed by it with very great rapidity, so that if planted in acid urine, the reaction becomes alkaline and the odour ammoniacal within a few hours.

Its pathogenic power varies with the kind of animal experimented upon, with the amount that is injected, and with the quantity of its own toxins that is injected with it. Very small quantities are apparently harmless in the case of rabbits. A larger amount injected subcutaneously, or (especially) into the substance of the muscles, is followed by suppuration and abscess. The products of a culture from which all the organisms have been filtered off, may prove rapidly fatal from toxæmia; and the same result follows if the culture itself is injected into the peritoneal cavity or into the circulation. Septicæmia appears only to follow in cases in which the tissues have been injured by some accidental violence, or by the simultaneous injection of a large dose of the toxic products. Under either of these conditions the bacillus is capable of multiplying indefinitely in the blood and in the tissues.

The streptococcus pyogenes is of not unfrequent occurrence in cases of cystitis, and as Melchior has pointed out, is always of grave import when it does occur. It spreads into the walls of the bladder, invades the mucous and submucous layers, and everywhere gives rise to suppuration. It is especially frequent, according to Hallé, in those cases in which phlebitis is present.

The streptococcus pyogenes does not possess the power of decomposing urea. When it is present in ammoniacal urine, the decomposition is due to some other organism, such as the urobacillus. It does not liquefy gelatin, and forms an almost imperceptible growth upon the surface, quite unlike the masses built up by the bacillus coli. It is, as its name implies, intensely pyogenic, causing diffuse inflammation and suppuration; and though very small injections of it into the blood-stream or the peritoneal cavity may not be followed by any ill-effect, larger ones rapidly prove fatal either from the direct action of the toxins it produces, or from septicæmia.

The staphylococcus pyogenes aureus, like the streptococcus, is too well known to need description. It decomposes urea readily and is therefore generally found in advanced cases of cystitis. Like the streptococcus, it is intensely septic and pyogenic, though the suppuration, when due to it alone, rarely assumes such a diffuse form; and if injected into the blood or the peritoneal cavity under conditions that favour its growth, it is equally powerful in causing septicæmia.

The fact that these organisms, or in rare instances, others closely resembling them, are invariably present in the urine in every case of suppurative cystitis, is not in itself sufficient to prove that they are the cause of the inflammation. This can only be shown by experiment. The injection of a pure culture into the bladder must invariably be followed by cystitis.

This is not the case. A pure culture of the urobacillus generally succeeds it is true; but if the bladder is healthy and uninjured, a simple injection of the bacillus coli almost always fails. Within a day or two, sometimes within a few hours, the organism completely disappears from the bladder, and the urine becomes as sterile as it was before. Barlow and Schnitzler alone have succeeded, by using an exceedingly virulent culture and injecting a large amount.

Some other condition is required. There must be retention of urine, or congestion of the neck of the bladder, or irritation of the mucous membrane, caused by mechanical or chemical irritants. Then, under these conditions, the injection never fails.

The reason why the urobacillus is sufficient of itself, while the bacillus coli is not, is that the former gives rise to ammoniacal decomposition of urine in the bladder, and the latter does not. The ammonia is a sufficient irritant.

Experiments that furnish definite proof of this have been performed by many observers in France and Germany. A ligature has been placed around the penis so as to cause retention of urine, the mucous membrane of the bladder has been bruised or cut, acute congestion of the neck of the bladder has been caused by the administration of cantharides or the injection of ammonia, and the result has always been the same. If no micro-organisms found their way into the bladder it rapidly recovered; the injury was repaired and the irritation disappeared. If on the other hand a culture in broth or urine was injected by means of a catheter introduced with the greatest care, or by means of a hypodermic syringe passed through the wall of the bladder, inflammation and suppuration invariably followed.

Clinical evidence is equally conclusive. Bacteria, even pyogenic ones, may pass through the bladder in myriads, as Guyon has shown, or may live in it for months, as in cases of bacteriuria, without exciting a trace of inflammation. Retention of urine, as in some cases of enlargement of the prostate, may continue for years and never cause inflammation. But if the two occur together, if micro-organisms gain entrance through a septic catheter, or through any other medium, in a case in which urine is retained in the bladder, suppurative cystitis always follows.

THE SYMPTOMS OF SUPPURATIVE CYSTITIS.

In suppurative cystitis the bladder contains myriads of septic organisms which grow and thrive in the urine and pour their poisonous products into it. If the attack lasts for any length of time, or if the micro-organisms are assisted by the presence of some additional irritant, such as a foreign body or a calculus, they spread through the protecting epithelial layer and involve the wall of the bladder too. And sooner or later, they extend up the ureter and attack the pelvis of the kidney.

The effect upon the bladder has been described already. That produced upon the kidneys depends in the same way upon the nature and virulence of the organisms that are at work and upon the accessory causes that assist them. If the outflow down the ureter is unimpeded, and nothing happens to cause renal congestion or irritation, a slow process of fibroid degeneration sets in; the kidneys become smaller and harder; the cortical substance wastes; and the surface becomes finely granular (Albarran, *Etude sur le Rein des Urinaires*, Paris, 1889, has shown how pyogenic organisms which are not sufficiently active to cause suppuration in the kidney, lead, in course of time, to a condition of sclerosis, identical with that which results from chronic interstitial nephritis). But if at any time the descent of the urine is checked, as it is in cases of vesical retention; or if the kidney becomes congested from cold or any other cause, suppurative pyelitis and nephritis follow, as surely as suppurative cystitis does in the case of the bladder.

The symptoms, therefore, in suppurative cystitis may be divided into local and constitutional. The former are caused by the irritation of the surface of the bladder.

The latter are partly direct, arising from the entrance into the circulation of the toxins produced by the septic organisms growing in the bladder; partly indirect, due to secondary affections arising as consequences from the cystitis, such as interstitial nephritis, suppurative pyelitis, and general septic infection. With these last I am not concerned at present, as it would be manifestly impossible to discuss them adequately in the space at my command.

Local Symptoms.

The local symptoms of suppurative cystitis are increased frequency of micturition, pain, and tenderness on pressure over the bladder.

The nerves distributed to the mucous membrane lining the neck of the bladder are, normally, as insensitive to the contact of urine as those of the corneal conjunctiva are to light. The stimulus that excites micturition is the tension of the walls of the bladder. When inflammation sets in the conditions are entirely changed, and the contact of the urine becomes as powerful a stimulus as the tension. Even in the slightest cases, where the epithelium is still intact, the nerves are intensely irritable. If there is the least abrasion of the surface, the effects are as marked as those that are caused in the eye by light falling upon a phlyctenular ulcer. The contact of the urine with the mucous membrane at the neck causes violent contraction. As soon as a few drops collect, they are ejected with a force over which the patient has no control, and which is accompanied by intense burning pain. Increased frequency of micturition is present in many other disorders, inflammation of the pelvis of the kidney, for example; but it is never attended in these cases by the strangury that is present in suppurative cystitis.

The pain that accompanies cystitis is due partly to the contact of the urine with the inflamed and tender mucous surface, partly to the tension of the walls of the bladder. Even when it is healthy the bladder is exceedingly sensitive to tension. When it is inflamed, its sensitiveness becomes so great that the least action of the muscles causes acute suffering. The more frequently they contract, the greater the pain becomes; and it reaches its maximum as the last few drops of urine are expelled. In most instances there is then a short respite, until the urine has begun to collect again. When, however, the attack is acute, the pain scarcely ever ceases. A drachm or two of blood-stained urine is expelled every few minutes. Violent spasms follow each other in rapid succession. The pain radiates in all directions, over the pubes, into the perineum and down the thighs. The muscles around the anus become involved as well, leading to the involuntary evacuation of fæces, and then to prolapse of the rectum. And at length the strongest endurance is broken down.

Normally, the bladder is almost insensitive to pressure, though it is most sensitive to tension. Its tolerance of large calculi is notorious. Pressure over the pubes, unless the bladder contains urine, does not cause pain. And after the neck of the bladder has been passed, the contact of a sound with the mucous membrane is scarcely felt. In cystitis all this is changed. The pressure of the finger in the rectum, or the vagina, is most painful. Bimanual examination in a case of acute cystitis is useless without an anæsthetic. If a sound is passed, the bladder contracts around it almost as soon as it enters. And even the pressure caused by the contraction of the muscles of the abdominal wall cannot be borne. The attitude of cystitis is characteristic. The patient, even if the bladder is empty, so that there can be no question of tension, stoops forward as he walks, often pressing his hands upon the abdomen, and moves with the greatest care.

CONSTITUTIONAL SYMPTOMS.

The constitutional symptoms in suppurative inflammation of the bladder are caused by the absorption from the urinary organs, kidneys as well as bladder, of the poisonous substances that are formed by the micro-organisms growing in the urine and in the tissues. Their severity depends upon the amount that finds its way into the general circulation, and the rapidity with which it enters. If the urine only is infected and not the walls of the bladder; and if the bladder is able to empty itself thoroughly, as it is in the majority of instances, the constitutional disturbance is not great. (Runeberg's case of bacteriuria (p. 43), and some of those related by Krogius, must be regarded as exceptional). There is no time for absorption to take place. The increased frequency of micturition which is so characteristic of cystitis is the safeguard of the bladder.

If on the other hand, the bladder has lost the power of emptying itself; or if the pyogenic organisms have penetrated through the epithelial layer, and invaded the wall of the bladder: still more, if from injury or any other cause, the perivesical tissues have become involved, the symptoms that follow may be of the gravest character. I have known a case in which a patient carelessly left in his bladder part of a septic catheter that he had passed upon himself, prove fatal from septic poisoning within a week. An opening was made through the perinæum, the catheter extracted, and the bladder drained, as soon as the facts of the case were known. But the temperature continued to rise; repeated rigors followed, and the patient became delirious and died two days later. There was no suppression of urine, and there were no local symptoms, apart from those presented by the urinary organs. The patient was poisoned by the absorption through the wall of the inflamed and ulcerated bladder, of the intensely offensive products of the organisms that were growing in the urine.

Acute Cystitis. The constitutional symptoms in acute inflammation of the bladder, vary in different cases, like those of general peritonitis and other forms of septic inflammation. In some instances there is fever high in proportion to the severity of the attack. In others, the temperature is scarcely raised above the normal. And in others again the patient sinks from what is often called exhaustion.

Sthenic inflammation of great severity is seldom met with in suppurative cystitis, unless it is complicated by inflammation of neighbouring organs. The bladder keeps itself empty, so that there is little absorption. But in young subjects, in the full vigour of life, I have known very acute symptoms follow when the exit from the bladder was obstructed, so that the urine could not escape. The attack may set in with a single rigor, or there may be a succession of them. The temperature may rise to 104° F. or even higher, and remain high, without falling to normal in the intervals. The pulse is full and bounding. The respiration is hurried. There is violent headache, often attended with vomiting. The face is flushed. The tongue is thickly coated ; the bowels are confined ; there is complete loss of appetite ; and, in a word, all the symptoms of acute septic poisoning. The worst cases, I believe, occur with a mixed infection, when, for instance, the bacillus coli is associated with the urobacillus liquefaciens septicus or the staphylococcus pyogenes. Under these conditions the urea is decomposed in the bladder, and the ammonia that is set free helps to break down the protecting layer of epithelium.

As soon as the bladder is emptied and allowed to drain absorption ceases and the symptoms begin to subside. If by any chance this does not take place, if the obstruction at the exit is not completely removed or evaded in some way ; or if as in the case mentioned above, there is some foreign body causing ulceration, absorption continues; the septic organisms penetrate farther and farther; the symptoms grow more and more severe, and if death does not ensue in the course of a few days from septic intoxication, the organisms gain the general circulation and septic infection follows.

The adynamic type is more common. It is met with especially in old men, suffering from enlargement of the prostate, at the beginning of what is called catheter life. The symptoms at first are very ill-defined. There is seldom any definite rigor, but there may be numerous slight chills. The temperature is but little higher than normal. The pulse becomes rapid and feeble. The tongue grows red and dry. There is complete anorexia. Delirium sets in at night, and in a considerable proportion of cases the symptoms progress steadily from bad to worse, until at the end of ten days or a fortnight the patient sinks into a semi-comatose condition from which he never rallies.

The symptoms in these cases are not due to cystitis alone. They are always complicated by those arising from the septic pyelo-nephritis that is invariably present at the same time. They are the product, not only of septic absorption from the walls of the bladder, but of chronic uræmia and septic absorption from the inflamed kidneys as well; and in any individual case it is impossible to apportion correctly the share that is due to each. For this reason they will be dealt with later, as one of the varieties of so-called "urinary fever."

In chronic cystitis the constitutional symptoms are much less severe. Unless the surface is ulcerated very little absorption takes place. Morphia, for example, may be injected into a bladder affected with chronic cystitis without producing the least effect. It does not even diminish the irritability of the mucous membrane. And the same thing is true of the toxins that are produced by the growth of septic organisms in the urine.

The epithelial cells when inflammation of the bladder has lasted some length of time are ill-formed and misshapen; but the layers grow thicker and the protective power is but little diminished. Persistent slight irritation makes the mucous membrane harder and more dense. Unless the surface is injured in some way, either by the bruising of a calculus, or by the action of some irritant, such as ammonia, there is little or no absorption in chronic cystitis, and no fever. When constitutional symptoms do make their appearance, they are for the most part the result of the secondary changes induced in the kidneys.

As might be expected, the symptoms are gravest when an acute attack suddenly breaks out in a bladder that has been affected for some years with chronic inflammation. This is not unfrequently the immediate cause of the end in cases of stricture and enlargement of the prostate. Some organism capable of breaking up urea finds its way in. Ammoniacal decomposition follows. The additional irritant, acting upon tissues that have been already injured by long-continued chronic inflammation, sets up an intensely acute attack; the kidneys rapidly become involved, if they were not affected already; and symptoms of septic poisoning follow as a natural consequence.

URINARY FEVER.

All operations upon the urinary organs (even such an apparently trivial matter as the passage of a sound or catheter into the bladder) are liable to be followed by consequences of a very serious kind. Some of these consequences, such as suppression and retention of urine, are in no way peculiar. They are due to shock affecting the nervous system generally, or those parts of it that are in immediate physiological relation with the injured structures. They may occur more frequently after operations upon these organs, than after those performed upon other parts of the body; but they are not peculiar to them. Others, such as suppuration, thrombosis of the veins of the prostatic plexus, pyæmia, &c., are due to infection by the ordinary pyogenic organisms, and occur in the same way that they do after operations performed upon other structures, in which it is not possible to avoid the danger of septic contamination. But these are not all. There are certain consequences of a very striking character, that never occur excepting as a result of some interference with the urinary organs. Operations performed upon other organs are exempt from them. For this reason, and because they are mainly the product of the action of the micro-organisms that cause inflammation of the bladder, they appear to me to deserve consideration here.

The clinical pictures presented by these cases differ very widely from each other. Some, however, are sufficiently distinct to stand out as types, and around these most of the rest may be grouped.

1. The most common form is characterised by the occurrence of a simple rigor, or more rarely, of more than one, but without fever or other cause for anxiety in the intervals. The urine always contains bacteria and nearly

always the bacillus coli. The bladder and kidneys may be perfectly healthy.

2. In another the prominent feature is profound collapse, which may terminate fatally within thirty-six hours. There may or may not be a rigor. The only instances of this with which I am acquainted have occurred after operations upon the kidney for septic pyelitis. I have not met with it after operations upon the bladder or urethra.

These two are dependent upon the same cause. They are examples of toxæmia, and are due to the sudden entrance into the circulation, through a wound, of the products of septic organisms growing in the urine or the walls of the urinary passages. The difference depends upon the dose and the rapidity with which it enters the circulation.

3. The third form of so-called urinary fever is very different. The symptoms do not follow at once. They set in quietly and insidiously, three or four days after the operation. There is no rigor, and there may be no fever, though a slight rise of temperature with occasional chills is more common. The pulse is frequent and feeble. The tongue, dry and red from the outset, soon becomes brown. There is complete anorexia. Wandering delirium sets in at night, and in a few days' time the patient sinks from what is commonly called exhaustion.

Cases of this kind are chiefly met with in old men, suffering from enlargement of the prostate, at the beginning of catheter life. No lesion or injury of any kind is necessary. Suppurative cystitis is the beginning. The urine is filled with septic organisms pouring their poisonous products into it. Ascending pyelitis follows. The septic organisms multiply with inconceivable rapidity, spread up the ureters and invade the pelvis of the kidney and then the kidney itself. The symptoms are the joint product of the septic poisoning arising from the absorption of the toxins that are poured into the urine and the tissues of the urinary organs, and of the inflammation of the kidneys caused by the invasion of the organisms themselves.

The suppression of urine in many of these cases is the most prominent feature, but there can be little doubt that in the majority the actual cause of death is the septic poisoning.

4. The fourth variety is different again both in its symptoms and its pathology. It is characterised by continued fever, with rigors that often occur at intervals as regular as the shivering fits of ague. It may set in almost at once, or not for days. It is quite independent of the state of the bladder or the kidneys. The urine is always loaded with organisms (in one case under my care it was an almost pure cultivation of the bacillus coli) ; and the symptoms are due to septic infection, not only the poisonous products of the organisms, but the organisms themselves entering into the circulation.

It is generally stated that urinary fever is the result either of a functional and transitory or of an organic lesion of the kidneys. That form, for example, of which a single rigor or a succession of rigors, without further effect, is the main feature, is assigned to reflex irritation of the renal nerves. Another is the result of acute interstitial nephritis, and another again is due to the outbreak of ascending pyelonephritis.

I am willing to admit that urinary fever of all kinds is more liable to occur in those whose kidneys are diseased, and who suffer from renal inadequacy, than in those in whom they are sound ; and undoubtedly, in one of the types that I have described above, the symptoms are largely due to the action of septic organisms upon the kidneys. But so far as the others are concerned, there is absolutely no proof that they are in any way dependent upon lesions of the kidneys, whether functional and transitory, or organic. Urinary rigors, for example, I have many times known occur in those whose kidneys were perfectly sound at the time, and have remained sound for years afterwards; and there is certainly no direct connection of any kind between renal disease and septic infection.

Nor is the difficulty surmounted by the suggestion that the lesion of the kidney may be a functional and transitory one. The passage of a catheter, or some other operation upon the urinary organs, is supposed to act as an overpowering stimulus. The renal nerves are paralysed for a time by reflex inhibition of the vaso-motor centre in the spinal cord; passive congestion follows, and this in its turn gives rise to urinary rigors and urinary fever.

As renal hæmaturia has been known to follow the passage of a catheter in one or two instances, it is possible that renal congestion may occasionally be caused in this way. Vaso-motor nerves can undoubtedly be inhibited by shock; and it may be granted that the passage of a catheter for the first time is a sufficient cause. But, admitting this, there is no evidence that renal congestion is often caused like this, or that when it does happen it can give rise to the symptoms I have described. All the evidence points in the other direction. Renal congestion due to such a chain of circumstances is a very rare event. I have scarcely ever met with a case in which there was the slightest proof of it. The symptoms that are produced by renal congestion, when it does occur, bear very little resemblance to those that are characteristic of urinary fever. The rigors of simple urinary fever are definitely associated with the act of micturition, and with the passage of urine under pressure over a recent wound. There is no evidence, in the vast majority of instances, either to show the existence of renal congestion, or to connect it when it is present with the occurrence of rigors. The theory of reflex irritation is a very unsatisfactory explanation, resting solely upon authority and not upon facts.

I. The simplest form of urinary fever is a single rigor. Rigors are chiefly met with after operations upon the kidneys in cases of septic pyelitis, and those performed upon the deep part of the male urethra. Suddenly, without any warning, or with only a slight quickening and perhaps irregularity of the pulse, the patient is seized with an unaccountable feeling of depression and anxiety. There is a strange sensation of coldness, which is often described as being felt inside. It may be only a slight chilliness, or it may be so intense that the bed is shaken by the patient's shivering. The skin is rough and wrinkled. The teeth keep on chattering. The natural colour disappears. A peculiar gray look comes over the face. The eyes become sunken and dark, and the aspect entirely altered. Meantime, while the patient is complaining of the most intense cold and that his hands and feet are like ice, the temperature rises until it reaches 105° or even 106° F. The pulse is hard and rapid. The respiration hurried and shallow, with a feeling of great oppression upon the chest. Often there is violent headache, with nausea, vomiting, and even in some cases delirium. Then, after a period varying from a few minutes to half an hour, the symptoms begin to change. The sensation of cold gives way to one of equally intense heat. The face becomes flushed, the eyes bright, and the skin hot and dry. The respiration becomes deeper, the pulse fuller and softer, and the sense of anxiety and depression less acute. By and by profuse perspiration sets in, in severe cases soaking the sheets and even the bed. A feeling of relief comes over the patient, and the temperature begins to fall, though it may be several hours before it reaches its former level. The next day, except for a feeling of prostration and weakness, there is no trace left.

In the majority of cases there is only one rigor. Convalescence proceeds without interruption. Exceptionally, there may be more than one. But when they recur, there is always reason to suspect that the case is not a simple one; and that more serious complications are present. And if no definite exciting cause can be found for the subsequent attacks, and the temperature between the rigors is not perfectly normal, the suspicion is probably well founded.

Rigors such as this are particularly common after operations for stricture involving the deep part of the male urethra. Those performed upon the penile portion enjoy much greater immunity; and they never occur after such a proceeding as division of the meatus. The rigors may follow simple exploration with a catheter, or dilatation, or internal urethrotomy. External urethrotomy is much less liable to be followed by them than internal. And I have many times known, while every attempt at passing a catheter was followed by a rigor, free division of the stricture put a stop to them once and for all.

Tying a catheter into the urethra may cause suppression of urine in either sex, women as well as men; but it does not increase the tendency to rigors. On the contrary, it often stops them, a fact that is absolutely inexplicable if rigors are caused by reflex irritation of the deep part of the urethra.

Operations upon recent strictures are more liable to be followed by rigors than those upon old and dense cartilaginous ones; and the frequency of their occurrence is very greatly influenced by the amount and the roughness of the manipulation to which the stricture is subjected.

Rigors are much more likely to occur in men who have lived much abroad; who have had attacks of ague, or intermittent fever; or who are suffering from insufficient renal action, than in those who are healthy. I believe, too, that under these conditions they are more severe. Their frequency is not influenced in the least by the degree of sensitiveness of the urethra, or by the administration of an anæsthetic.

The rigors that occur after operations for stricture rarely follow immediately. Nearly always they begin within half an hour after the first act of micturition; and the longer this is postponed, the less the risk. They may, however, be brought on the following day, or even the day after that, by any sudden chill. I have several times known them occasioned, after five or six acts of micturition by the patient, who had grown careless from immunity, getting out of bed to pass water and standing with bare feet upon boards or oil cloth. Late rigors such as these are generally of less intensity than those that occur shortly after an operation.

Rigors are by comparison, rare after operations upon the bladder. I have never known one occur after suprapubic cystotomy, but they sometimes follow when the incision is made in the perineum. The reason is probably to be found in the size and freedom of the opening and the consequent absence of urinary pressure.

On the other hand rigors are quite common after exploration of the kidneys in cases of septic pyelitis, and occur irrespectively of sex, as frequently in women as they do in men. They differ from urethral rigors in that they may begin immediately after the operation. I have known a patient who was suffering from septic pyelitis, for which it was thought advisable to drain the kidney, seized with a rigor before she had recovered from the anæsthetic. A second followed a few hours later, but neither had the least effect upon the patient's convalescence which progressed without interruption, from the first.

These rigors, whether they occur after operations upon the urethra, or upon the kidney, are identical in all important respects, and are dependent upon the same cause.

The difference in the length of time that intervenes between the operation and the rigor is easily accounted for. In cases of septic pyelitis the symptoms begin at once, because the poison that has collected in the pelvis of the kidney is driven by the manipulation directly into the torn and injured bloodvessels. On the other hand, in stricture of the urethra, there is no pressure upon the contents of the bladder, and no absorption until micturition takes place.

Cystotomy and external urethrotomy are, comparatively speaking, exempt from rigors. The wound is so large and free that there is no pressure.

Old cartilaginous strictures are also exempt, but for a different reason. The cellular tissue is so dense that absorption cannot take place.

These rigors are typical instances of what it is customary to call urinary fever.

There is no doubt that they are due to absorption of some of the constituents of the urine. They are frequent in proportion to the facilities that are offered for absorption. They are more likely to occur if there is a wound than if there is not. They are more common after operations upon the urethra than those upon the bladder. And they are more likely to follow when the urine is expelled under high pressure than when it is allowed to flow away.

It is equally certain that they are not due to the absorption or entrance into the circulation of any of the normal constitutents of the urine. Normal urine, if injected into the vessels in sufficient quantity, does, it is true, cause symptoms of poisoning, but only when the amount is excessive, and then the symptoms are not the same as these.

Their real cause is the septic condition of the urine and the septic poisons that it contains. In every case that I have examined in which there has been a rigor, septic organisms have been present in the urine, and almost invariably the bacillus coli. Sometimes it was alone: sometimes in association with others. Occasionally only one culture out of five or six succeeded. As a rule it was present in abundance.

If this organism is grown either in urine or in bouillon, and the toxins are extracted from the culture and injected into a rabbit's veins, symptoms of a closely similar character always follow.

The clearest proof, however, of the septic origin of these rigors is the fact that they can be prevented almost, if not entirely, by taking suitable precautions; by using, for example, antiseptics sufficiently strong to destroy, or at least to check the growth of the bacterium coli in the urine; and by keeping the bladder empty, so that the septic urine does not pass down the urethra under pressure.

The following is the plan I adopt myself, wherever it is practicable. Modifications of course are required to suit the needs of individual cases.

The first essential is to clear out the intestinal canal thoroughly. I do not mean to say that the bacillus that causes rigors always comes directly or indirectly from the intestine, though I am sure that it has done so in some cases. But there can be no question that the intestine is the chief nursing ground for it, and that it is eminently desirable to get this as clear as possible. For some days beforehand the patient is given two or three grains of salol, six or eight times in the twenty-four hours. If given in larger amounts the salol may melt and run together during digestion, and then, later, crystallise out again, and form an intestinal concretion. If the urine is alkaline from the presence of a fixed alkali, benzonaphthol is to be preferred, given in cachets, as it breaks up in the intestine into β-naphthol and benzoic acid. Three days before the operation the patient is given a calomel purge, followed by an effervescing draught; and again the night before. The amount of calomel can, of course, have little direct influence upon the growth of septic organisms in the intestines; but as to its value clinically I have not the slightest doubt.

The patient should be very warmly clad for the operation, especially if ether is given. There can be no question that cold can precipitate if it cannot cause a shivering fit.

Immediately before the operation the glans penis, prepuce and meatus, are thoroughly washed with soap and water, and then with corrosive sublimate solution, one in a thousand. The urethra itself is cleansed as perfectly as it can be with a boracic acid douche and a catheter that admits of a return current along the walls. It is impossible to get it quite aseptic; but by passing the catheter into the fossa navicularis and washing that out thoroughly; then pushing it in a little farther and repeating the process, and finally carrying it down to the face of the stricture, the anterior part of the urethra can be fairly well cleared. The portion behind the stricture is of course unapproachable at this period.

The instruments are sterilised and kept from contamination by wrapping them in a carbolised towel. As few as possible are used, and manipulation is reduced to the narrowest limits consistent with the effectual performance of the operation.

At the end of the operation the bladder is emptied by means of a catheter, and two drachms of a two per cent. solution of nitrate of silver injected into the deep part of the urethra and on to the face of the stricture, and left there. The nitrate is decomposed at once into the chloride, which is thrown down as an insoluble powder on the surface of the mucous membrane, acting as an effectual germicide.

Micturition should be postponed for as long as possible after the operation, in order that the surface of the wound may become glazed over; and the patient is not allowed under any circumstances to get out of bed or expose himself to the least chill.

If in spite of all these precautions rigors do occur after a stricture has been divided, further trouble can be prevented by injecting some nitrate of silver into the urethra at the seat of the stricture, and tying a catheter into the bladder. If rigors were really due to reflex irritation, the latter proceeding would make them worse. As a matter of fact, in conjunction with the nitrate of silver, it stops them by preventing further absorption.

All the other measures that are usually recommended, such as allowing the patient to empty his bladder while sitting in a hot bath, and giving hot tea, quinine, opium, and brandy, I have tried thoroughly; and I have come to the conclusion that though they may lessen the patient's discomfort when rigors actually occur, they do little or nothing in the way of preventing them.

These are the reasons why I regard urinary rigors as a form of septic poisoning, due mainly if not entirely to the bacillus coli. Normal urine injected into the blood-vessels does not cause them. Septic urine does. The presence of the bacillus can be demonstrated in the vast majority of cases, if not in all. This bacillus is undoubtedly capable of producing toxins of sufficient virulence, even when the dose is infinitesimally small. Everything that favours absorption increases the likelihood of rigors. Conversely, everything that checks it, tends to prevent them. And the most effectual method of stopping them altogether, one that rarely fails, is the injection of a powerful germicide on to the spot where it may be presumed the organism is most abundant, and absorption most likely to occur. It is a mistake to speak of rigors like these by the name of urinary fever—fever due to re-absorption of some of the constituents of the urine. It overlooks the true cause, gives an entirely wrong impression, and what is much more important, leads to a wrong method of treatment.

II. Operations upon the kidney in cases of septic pyelitis are occasionally followed by symptoms of a much graver character. Even before the effects of the anæsthetic have passed away, the condition of the patient may be such as to excite the most serious anxiety. There may be no sickness (or only such as can be accounted for by the anæsthetic), or fall in temperature, or rigor. The operation may not necessarily have been a long one, or one that would cause an unusual degree of shock. It may appear to have been perfectly successful. But the pulse becomes small and frequent; the face has a peculiarly dusky appearance; reaction does not set in; and though there is a complete return of consciousness, the patient lies in a listless state, as if the mental powers were overwhelmed. Sometimes this condition passes off; but on the other hand, it may prove fatal within the course of a few hours.

My attention was first drawn to this by a case that was under my own care four years ago. The patient was a young lady, fourteen years of age, tall and slightly built, who had suffered for some years, probably from infancy, from pyelitis accompanied by attacks of renal colic. These, though not of the severest character, had been sufficiently frequent to render her life a burden. The urine contained a distinct amount of pus, with occasionally a little blood. The quantity and specific gravity were both good. There was great tenderness on pressure over the tips of the last ribs on the left side. The right kidney could be felt, and was not more tender than usual.

On exploration, a very large branching calculus was removed, with several small ones, which may have been formed separately, or perhaps, were fragments broken off some time before. The pelvis and the calyces were carefully explored with sounds; but owing to the length of the patient's chest, the lower ribs almost reaching the ilium, and the mobility of the kidney, the upper part of the cavity could not be reached with the finger. Twenty hours after the operation a rigor followed, the temperature rising to 102° F.; and in the course of convalescence several more occurred. But by degrees the wound contracted to a sinus, the amount of discharge diminished and the temperature fell to normal.

The pain, however, did not disappear. That one telltale spot, opposite the tip of the eleventh rib, persisted. The slightest percussion there caused a sharp stab of pain, and it was evident that something had been left behind. Accordingly I explored the kidney a second time. The first operation was one of considerable difficulty. The patient's chest was very long; the kidney was completely covered by the ribs, and was very movable; and a great deal of manipulation was required to extract the stone. The second operation was as simple as such an operation can be. The kidney was fixed, and drawn much nearer to the surface by the cicatricial tissue that had formed around it. A sinus led down into the pelvis. All that was required was to dilate this sinus and introduce the finger into it. A small calculus was detected almost at once, lying in the upper part of the pelvis, in one of the calyces, and extracted without difficulty. The operation lasted a very short time; the patient was not chilled in the least, and there did not appear to be any reason why shock should be severe. In the evening it was noted that the extremities were warm and there was no fall in the temperature. The thermometer in the axilla marked 98° F. The next morning it was 101° F., and in the afternoon it had fallen again to 99° F. But the face was dusky; the pulse quick and running; a diffuse erythema had made its appearance over the lower part of the body and the thighs, and the patient died in the course of the evening, within thirty hours of the operation. There was no suppression of urine or vomiting. At the post-mortem examination all the viscera were more or less congested. The opposite kidney was healthy and sufficiently large. There was no evidence of peritonitis; and there was no hæmorrhage or thrombosis. The patient retained a certain degree of consciousness almost to the last; but lay perfectly quiet, with eyes half closed, scarcely answering when spoken to, and taking no notice of anything that was going on around. The condition, in short, was such as is sometimes seen in very severe cases of acute suppurative osteomyelitis—cases that prove fatal before any secondary pyæmic symptoms, such as pericarditis, have had time to develop.

Such cases are fortunately of rare occurrence. A few of a similar character have been recorded at various times by other surgeons; and they have been regarded by most as the result of shock. With this opinion, however, I am quite unable to agree. So far as I understand shock, the characteristic symptoms are entirely wanting.

Shock, I admit, is often very severe after operations upon the urinary organs, and especially upon the kidneys. I have been told by Dr. Hewitt that he has several times known the pulse to fail at the moment that the ligature was tightened around the pedicle in performing nephrectomy. The operation is a long one. The wound is of considerable depth. The semilunar ganglion is in close proximity; and the nerves of the renal plexus are often included in the loop thrown around the vessels. But the symptoms in this case were totally different from those of shock. In shock the temperature always falls. The extremities grow colder and colder. The face and lips are white, and the forehead covered with perspiration. The eyes are sunken, and surrounded by dusky rims. The nose is pinched; and the secretion of urine is either stopped altogether or falls far short of the normal. I cannot, therefore, regard this as a case of shock.

On the other hand there can be no question that septic poisons were present in the wound; that they were of the most virulent character; and that there was every facility for their absorption.

The mixture of pus and urine that filled the pelvis of the kidney, and overflowed into the sinus, was full of micro-organisms. They consisted for the most part of staphylococci, and a bacillus, which agreed with the bacillus coli in its mode of growth upon potato and gelatin, and the rapidity with which it coagulated milk. As usual when this bacillus is present in any numbers, the odour was decidedly fæcal. These organisms must have been growing in the pelvis of the kidney, in very favourable circumstances for some considerable time. The fluid therefore that filled it certainly contained some, probably a large amount, of their toxic products. And the operation was one that might very easily have resulted in forcing some of these products into the open ends of the torn vessels.

Nor can there be any doubt as to the virulent character of these toxins. Numerous experiments upon animals have been performed abroad by Melchior (*Cystite et Infection Urinaire*, 1895, p. 143), Gilbert (*Soc. de Biologie*, Feb. 25, 1893), and others; and they have shown conclusively that the most minute quantity injected into the circulation gives rise to fever with loss of appetite, apathy and diarrhœa; and that a quantity only slightly larger will cause dyspnœa, convulsions and fatal collapse. Sometimes there is high fever; sometimes a temperature below normal; and mixed toxins, such as were present in this case are often much more poisonous than would be expected from the effects they produce when acting separately.

All the conditions in short for the production of acute septic poisoning were present in this case; and I regard it as an instance, not of shock, or of urinary fever, but of acute septic intoxication due to the sudden entrance into the circulation of an overwhelming dose of mixed toxins at a time when it can easily be imagined the kidneys were not working at their best. The germs themselves may have entered too; it may have been a case of septic infection as well as of septic intoxication; but the symptoms set in with such rapidity and intensity that they would scarcely have been caused in this way. There was no time for incubation.

III. The third variety of so-called "urinary fever" differs entirely from the two former. No wound or lesion is necessary. It may follow a severe operation, but that which most often gives rise to it is the passage of catheters. The bladder is always inflamed and the kidneys are always diseased. As a rule chronic interstitial nephritis has been present for years. The final cause is an outbreak of suppurative cystitis extending upwards and giving rise to septic pyelonephritis. The symptoms are due in some measure to uræmia, but mainly to septic poisoning caused by the absorption and accumulation in the system of the toxins produced by the organisms that are growing in the urine and the urinary passages. Suppression of urine, partial or complete, may occur; but it is not an essential feature. I have known the opposite condition, polyuria, present in a considerable number of cases.

The most characteristic examples are met with in old men suffering from chronic interstitial nephritis and atony of the bladder, at the beginning of what has been called catheter life. The symptoms so far as their broader features are concerned, present but little variety. The urine is clear and free from pus. There is no cystitis or suppurative pyelitis. The reaction is faintly acid. The specific gravity is low and the quantity unusually large, considering that we have to deal with patients who if not bedridden are leading very quiet lives. The first introduction of a catheter does not, as a rule, give rise to any disturbance. Nothing even may be noticed for a week. But generally about the third or fourth day (if the catheter is passed every day) a certain degree of irritability is complained of about the neck of the bladder. There is a desire to pass water more frequently; and the call cannot be resisted. It must be obeyed at once. Then the urine is noticed to be slightly cloudy though it still remains acid; and now there may be a small quantity of albumin present, though it was not there a few days before. The total amount passed in twenty-four hours too begins to fluctuate. Sometimes it falls so low that there is reason to fear that suppression may follow. Sometimes, on the other hand, it increases until there is a veritable polyuria. In one patient under my care the amount rose to between seven and eight pints in the twenty-four hours, for many days together. Under the microscope there are a few hyaline casts; perhaps a blood corpuscle or two; pus corpuscles in abundance, and myriads of bacteria. If a culture is made, the bacterium coli is almost always present, and in a very large proportion of cases unmixed with any other.

Meanwhile the patient is feverish. There is seldom any definite rigor, but there may be numerous slight chills. The pulse grows more rapid and feeble. The tongue, red and dry at first, soon becomes brown. There is complete anorexia. Delirium sets in at night; and unless a change is effected at once, the symptoms grow worse and worse until at the end of ten days or a fortnight, the patient sinks into a semi-comatose state from which he never rallies.

If steps are taken sufficiently early to render the urine aseptic, and prevent further infection by thoroughly draining the bladder, the cystitis may subside and the symptoms disappear. But even when this occurs during the first few days, it is often many months before the patient regains his strength; and if the slightest precaution is neglected, relapse is certain.

Post-mortem, the bladder is generally large, with flaccid walls. Sometimes the muscular coat is thickened and fasciculated; more frequently it is thinner than natural, or very irregular. The mucous membrane is stained by old hæmorrhages, and may be almost slate-coloured; and the epithelium that covers it is detached in places, here and there, so that when it is examined under water with a magnifying glass, it appears slightly roughened and even villous. The ureters are dilated. The pelvis of the kidneys is in a similar condition to the bladder. The kidneys themselves are small and shrunken. The surface is irregular. The capsule is adherent. On cross section the cortex is thinner and harder than it should be; and even the pyramids are greatly wasted.

In addition, however, to these changes, which are to be regarded as evidence of the troubles of past years, there are always signs of recent acute inflammation as well. Here and there little flakes of pus are adherent to the epithelial lining. There are a few recent hæmorrhages among the older ones. On the more prominent parts, such as the edges of the folds, the epithelium is completely abraded. In the kidneys the apices of the pyramids show signs of erosion. And in places between the tubules and under the capsule there are minute collections of pus, differing in shape and outline according to the anatomical arrangement at that particular spot. In other words, suppurative cystitis and ascending pyelonephritis have been added to the changes that have been induced in the past years by mechanical obstruction to the exit of the urine and the other troubles that complicate the presence of residual urine.

If cultures are made from the urine in the bladder, or the pus that is found in the pelvis of the kidney or between the tubules, the same organism, the bacterium coli, is nearly always present, and in those cases in which the urine has continued to be acid, generally speaking as a pure cultivation.

Many years ago Sir Benjamin Brodie drew attention to these cases; and since then they have been described by Sir Henry Thompson and by many others; and by nearly every one, the symptoms have been assigned to the suddenness with which the change is made from the natural and usual mode of micturition to the artificial one. Removing the whole of the residual urine at once, on every occasion of catheterism is most injurious during the first few days. "If the patient has been in the habit of retaining perhaps a pint of urine, or even more, after he has made water, it is a serious change for the bladder to be suddenly and completely emptied two or three times a day; the organ soon becomes irritable, the urine is charged with pus, and the patient loses appetite and becomes feverish, and there is sometimes considerable danger to life. The rule under such circumstances is to proceed cautiously. Instead of removing the entire quantity, leave some urine behind; and thus a compromise is made between the exigencies arising in this condition of the bladder, and the usually absolute rule that it should be emptied. Draw off a half or only two-thirds of a pint; you will thus relieve the organ partially, and in the course of a week or sooner, you may gradually accomplish the entire emptying of the bladder, and all will probably go well. And it conduces greatly to success to permit no out-door movement to such a patient, but to confine him to his room, in a warm temperature, if the weather be cold, or even to his bed for a few days," (*Clinical Lectures on Diseases of the Urinary Organs*, Sir H. Thompson, 6th edit., sect. x. p. 56). In the light, however, of the results arrived at by recent bacteriological researches into the causation of cystitis, I cannot help regarding the explanation as inadequate and unsatisfactory. I do not believe that emptying the bladder is the cause.

I do not for a moment deny that rapidly drawing off a large quantity of residual urine through a large catheter while the patient is standing upright, would be followed by syncope, and very likely, as patients who suffer from a large amount of residual urine are almost all of them aged and broken down in health, by sudden death; but these cases are not to the point. They present no resemblance in their clinical history, or their pathology, to those that I have in hand; and I am happy to say they must be very rare. I have not only never seen one, but I have never heard of such an instance, either at hospital or in private practice.

Shock will not account for the symptoms or for the pathological changes. The shock that follows operations upon the urinary organs is always immediate in its action. It may affect either the whole nervous system, or only those parts of it that are in close physiological relation with the nerves of the injured structures. In the former case the patient falls at once into a state of collapse; the functional activity of every organ in the body is suspended more or less completely; and the kidneys and the bladder suffer with the rest. In the latter, the kidneys and bladder suffer chiefly, if not exclusively. While other organs are but little affected, these lose their power of working, and either suppression or retention of urine follows, according as the influence of the shock falls more heavily upon the nerves that control the kidneys, or those that control the bladder.

Now the troubles that are caused by the evacuation of residual urine (except in those cases which I have already excluded) never begin at once. There is always an interval, always of some days, sometimes of more than a week; and when they do set in, they begin, not suddenly, but quietly and insidiously. They cannot therefore be due to shock.

Nor are they due to suppression. In the first place because in many instances there is no suppression, but exactly the opposite condition, polyuria. I have met with this on several occasions; in one case the quantity passed in twenty-four hours rose to between seven and eight pints. And in the second place because the symptoms that are present in these cases bear but a very remote resemblance to those that occur in true suppression of urine, such for example, as that which is caused by obstruction of the ureters. Total suppression may continue for ten or even fifteen days before it proves fatal. In many instances there are no symptoms at all for the first seven or eight. When they do set in there is no continued fever, or rigors, or delirium. Failure of muscular power and weakness of the pulse are the characteristic features. Consciousness is retained to the last. The symptoms in these cases, therefore, cannot be due to suppression, although it is quite possible that when there is partial suppression, they are aggravated and complicated by it. Naturally, if the toxins that are absorbed from the urinary passages are not excreted by the kidneys, they accumulate in the blood, together with other deleterious substances that should be got rid of in the same way, and produce a proportionately greater effect.

On the other hand, these symptoms are identical in every respect with those that occur after operations performed upon the same kind of patient if the wounds become septic. The gradual onset, the condition of the pulse and tongue, the delirium at night, and the steadily advancing weakness without any marked degree of fever, are exactly what is met with in the so-called exhaustion that proves the end of so many septic operations in the aged. The symptoms are identical in other words with those of slow septic poisoning; and they are due to the gradual absorption of the toxic products of the organisms growing in the urine and on the walls of the urinary passages. They may be modified by the failure in the excretory power of the kidneys, which prevents the system getting rid of the poisons as rapidly as it should; but the essential cause is the absorption.

In all these cases the first symptom is the same. Suppurative cystitis, manifested by turbidity of the urine and irritability of the bladder, is always the beginning; and this is always due to septic organisms. I have examined the urine from a very large number of these cases, and septic organisms are always present, generally the bacillus coli, sometimes alone, sometimes in conjunction with others. Suppurative cystitis never occurs without them. The entry of septic organisms into the bladder is the starting point.

These organisms do not get in by themselves. Residual urine may exist for many years without their getting in, or cystitis taking place. They do not get in until a catheter is passed, and they get in then because they are carried in by the catheter. A catheter that has never been used is sometimes aseptic. After it has been used two or three times, and has been cleaned in the ordinary way, it is never sterile.

Two facts bear out this statement very strongly. One is that these consequences rarely set in if a catheter is only passed once. They do not set in until the instrument has been used three or four times—until, in other words, it has become septic, and the organisms have had time to grow in the urine. The other is that they very rarely occur at all in cases in which catheters are never passed. They do not occur when a bladder is drained through the perinæum, or when an aspirator is used, even if it is used four or five times successively, provided, that is to say, that at the end of that time the patient has so far regained control over his bladder that a catheter is not required afterwards. I have notes of fourteen cases of complete retention in which an aspirator was used, and the bladder emptied as thoroughly as possible ; but no consequence of this kind followed in any one of them. The cause of the symptoms is not the emptying of the bladder. They cannot be accounted for by shock, or by suppression of urine, or reflex congestion of the kidneys. They are dependent upon the use of catheters, and in some other way than through the reflex action of the nervous system.

As soon as these organisms enter the bladder, suppurative cystitis follows. Nothing is more favourable to their growth than stagnant urine, mixed with a trace of albumin, kept at the temperature of the body. In a very little while they convert the contents of the bladder from a comparatively harmless fluid into an intensely poisonous one. Under ordinary circumstances when the bladder can empty itself thoroughly and at frequent intervals, their entry is not a matter of such serious moment. The frequency of micturition which is so invariable in cystitis is a perfectly adequate protection. But in these cases the bladder has lost the power of emptying itself ; a certain amount of urine always remains behind; and the result is the same as when there is any other ill-drained suppurating cavity, full of septic organisms. No sooner have the organisms begun to grow than they spread up the ureters, and involve the pelvis of the kidneys. The walls of the ureters in these cases are almost always thin and flaccid. The calibre is often wider than natural. The valve at the entrance into the bladder does not act; and owing to the degenerative changes already present, the tissues themselves are incapable of making an effectual resistance. In a very little while the micro-organisms spread in all directions through the kidneys, and wherever they make their appearance, suppuration and septic absorption rapidly follow. There is no rigor or conspicuous rise of temperature because the poisoning is so gradual; but in all other respects the symptoms are identical with those that occur when septic intoxication takes place from other causes in patients of a similar description.

Whose fault is it that these organisms get in? Do they come from the urethra, swept in by the catheter? or is the catheter septic before it enters the meatus? I am sure that in the majority of cases the fault is in the catheter. It is true that the urethra always contains germs, and that they cling to it so closely that it is almost impossible to render it sterile by washing it out; but these germs are for the most part non-pathogenic. Their presence does not matter if they do happen to be carried into the bladder. As soon as the urethra becomes inflamed there are septic organisms in abundance; but inflammation of the urethra is rare under these conditions unless it has already been caused by instrumentation. In the vast majority of cases the catheter itself is to blame. No one would think of using a scalpel that had been used already on a septic case, or on any case at all, without having it thoroughly sterilised first. Yet, though catheters are much more complicated instruments, and though every case of cystitis, no matter how slight it is, is septic, catheters are used again and again, with only the most perfunctory cleaning.

There are of course accessory causes. Chronic interstitial nephritis, for example, is always present when there is much residual urine. In most instances, at the time when catheter-life is commenced, it is already far advanced. The general health, therefore, is always impaired, and the excretion of waste products imperfectly carried out. But the time and the way in which the symptoms set in render mistake out of the question. The broad fact remains that the entrance of the organisms and the beginning of the symptoms are coincident with the use of the catheter.

These consequences may be avoided with almost absolute certainty if proper precautions are taken and catheters are sterilised as they ought to be, even though the bladder is emptied thoroughly.

I look upon the evacuation of a large amount of residual urine as a serious surgical proceeding, requiring the same precautions that are adopted in the case of any other surgical operation. The patient should be prepared in the way I have described already. The hands, the glans penis, the prepuce, and especially the meatus are thoroughly washed with soap and water, and then with a disinfectant that can be relied upon. I prefer corrosive sublimate, one part in a thousand. Every instrument is boiled and wrapped in carbolised lint. The lubricant is sterilised. (It is no use adding an antiseptic. If the antiseptic is a weak one, it does no good. If it is strong enough to be of any use as a germicide, it injures the mucous membrane of the urethra). I prefer Melchior's catheter, with one of my own, made for me by Messrs. Maw, Son and Thompson, as the inner of the two. The whole of the urine is allowed to drain away quietly, without using any pressure upon the bladder. If the amount is large this often takes some time as the inner catheter is only a No. 5 English. And this is done twice a day until the bladder has begun to recover some degree of tone, the patient meanwhile, as in the case of every other serious surgical operation, being confined to bed. Every day a culture is made from the urine, selecting the last portion passed; and if on the following day there is the faintest suspicion of a growth (it is quite possible to detect it in twenty-four hours, if the temperature is kept up), or if the urine is cloudy, or if there is any sign of irritability of the bladder, some nitrate of silver is injected into the neck; and if this does not stop the growth at once, the bladder is kept empty, either by tying a catheter into the urethra, or by incision according to the circumstances of the case. Germs are not capable of much harm in a bladder that is kept empty.

The real danger is not in emptying the bladder, but in failing to do so. The walls are flaccid and toneless; and if the urine is allowed to escape rapidly they collapse, like those of a thin walled inelastic bag, and fall into a number of folds between which a certain amount of urine collects ready to become a virulent poison, if only the germs can get in.

IV. There is one more definite variety of so-called urinary fever. The symptoms present a superficial resemblance to those of the one that I described first, especially to that form of it in which rigors recur at intervals. In this, too, rigors are present. But they do not begin on the first day. They occur without any definite exciting cause, sometimes irregularly, sometimes at intervals so regular as to suggest an attack of intermittent fever. They bear no relation to the act of micturition. The temperature is not normal in the intervals; and they are accompanied by other evidence of constitutional infection.

These cases are fortunately rare. They may occur after operations upon the urethra, bladder, or kidneys. One of the most striking I have seen followed the removal of a polypoid outgrowth from the neck of the bladder in a man, apparently perfectly healthy, 58 years of age. There was a large amount of residual urine, at times amounting to as much as a pint, owing to the growth acting like a ball valve, falling into and completely closing the outlet. The pedicle which was very narrow was twisted off through a median perineal incision. There was little or no external hæmorrhage, but evidently, as often happens in these instances, there was considerable oozing afterwards, and coagula formed in the bladder. For the first three days everything went well. There was some difficulty in micturition, owing to the coagula, but not sufficient to require the passage of a catheter. Then a rigor occurred, and the temperature did not fall to its former level after the shivering had passed. The next day there was another rigor; and from that time until the patient died three weeks later, the temperature chart never ceased to exhibit the most exaggerated oscillations. There were no local symptoms with the exception of an attack of diarrhœa lasting for some days, during which the motions were intensely offensive; and, three days before the end, thrombosis of one of the popliteal veins. The wound progressed perfectly and was almost healed at the time of death. The power of voluntary micturition and emptying the bladder was regained. The urine remained acid throughout, even when the coagula were present. The quantity and the specific gravity were good; and there was no albuminuria after the blood had disappeared. But the strength failed more and more. The body became extremely emaciated. The face assumed the characteristic jaundiced appearance; and at last a condition of stupor supervened.

Unfortunately the blood in this case was not examined. (The bacillus coli has been found in the blood in many cases. Sittmann and Barlow, for example, *Deut. Arch. f. Klin. Med.*, 1894, vol. 52, p. 520, describe it as present in the case of a man who died from chronic cystitis, pyelonephritis and endocarditis; and other instances have been recorded by Hartmann, Clado and Albarran). There can, however, be no doubt that the immediate cause of this patient's death was septic infection, and that this was due to the entrance into the circulation of an exceptionally virulent form of the bacterium coli.

The circumstances of the operation were such as to admit of the possibility of a large number of these bacteria entering at the same time. There was free venous hæmorrhage; and owing to the obstruction caused by the coagula at the neck of the bladder, the pressure in the bladder must have been raised considerably during micturition. The urine was loaded with the bacterium coli. It was examined many times but no other organisms worth mentioning were present in it. The reaction was strongly acid throughout, and it contained a quantity of indol. Where the bacteria came from cannot be said. The usual source is the intestine, directly or indirectly; and from the particularly offensive character of the stools in this case, there can be little doubt that the bacteria that inhabited the colon were of an especially active type.

It is true, as I have mentioned already (p. 56), that the bacterium coli does not readily give rise to septicæmia. The circumstances must be exceptionally favourable. An intermuscular injection, for example, in the case of rabbits, is not followed by general infection. It merely gives rise to local suppuration. But when the conditions are suitable, the bacterium coli is capable of causing a most acute form. If other organisms are present as well; or if a large amount of its own toxic products are injected into the veins at the same time, there is hardly an organism that surpasses it in activity or virulence.

Cases of septic infection, such as this, following operations upon the urinary organs, are happily very uncommon. But it seems probable that many of the instances of so-called urinary fever, in which prolonged illness, with frequent rigors, and no definite local cause, has followed internal urethrotomy and other similar measures, are really due to general infection. Either the virulence of the organism is less (there is evidence to show that this varies a great deal), or the resisting power of the blood and the tissues is greater, and the patient after a time recovers.

I do not wish to assert that all the cases in which febrile symptoms occur after operations upon the urinary organs admit of being grouped in this way, and classified under one or other of the foregoing heads. The cases that I have mentioned as illustrations have been selected as types from the notes of several hundreds, because they were uncomplicated in a singular degree by the troubles that are ordinarily caused by septic organisms; and because, in them, the condition of the kidneys was known, and there could be no doubt as to the share that they took in the causation of the symptoms. In the majority of instances the symptoms are so mixed and confused with those of chronic interstitial nephritis and ascending septic pyelitis that it is next to impossible to unravel them and assign each to its cause.

Of the four varieties that I have described, only the two first can in any way be included under the heading of urinary fever—fever due to the entrance of some of the constituents (abnormal it is true) of the urine into the blood. The third should be described as cystitis and ascending or septic pyelonephritis. The fourth is septic infection.

The one feature that is common to them all is, not the condition of the kidneys, whether they are diseased or not, but the presence of septic organisms in the urine, and particularly the presence of the bacterium coli. The reason why this organism has hitherto attracted so little attention in connection with diseases of the urinary organs is that it has hardly any effect upon the reaction of the urine. The urine has remained acid and therefore has been thought to be free from contamination. It cannot be too strongly affirmed that the most active septic organisms, capable of producing poisons so virulent that, if injected into the system even in infinitesimal quantities, they speedily cause death, may grow and thrive in urine that is highly acid, without effecting any appreciable change in its reaction.

ON THE WAY IN WHICH MICRO-ORGANISMS GAIN ACCESS TO THE BLADDER.

There are four distinct routes by which the bladder may become infected. Micro-organisms may enter the bladder directly through the urethra. They may descend with the urine from the kidneys. They may be brought to the bladder by the blood-vessels and attack the mucous membrane directly. Or they may find their way into the wall of the bladder by extension along the lymphatics from some of the neighbouring organs.

In considering this question I shall confine myself almost entirely to the bacillus coli. It is the most frequent cause of cystitis and pyelonephritis; and it is more easily traced than some of the other organisms that are so often present with it.

Its chief habitat, as its name implies, is the intestine. Except perhaps in newly born infants, it is never absent, though as I have shown, cultures of it taken from the intestine under different circumstances, appear to vary greatly in virulence.

In the male sex, cultures of different kinds of organisms can always be obtained from the surface of the glans penis, the prepuce and the fossa navicularis. As a rule they are mixed cultures, many of the organisms being non-pathogenic. But the bacillus coli is present in a very large proportion.

In women, the neighbourhood of the meatus urinarius is never free from micro-organisms, and cultures of the bacillus coli, mixed with others, can nearly always be obtained from it.

With regard to the deep portion of the male urethra, it is still uncertain, whether, so long as it is healthy, it harbours pathogenic organisms for any length of time.

Rovsing, it is true, found in the urethra all the organisms that he described as present in cystitis, thus confirming the conclusion at which Lustgarten and Mannaberg had already arrived. But on the other hand, Petit and Wassermann (*Ann. des Mal. des Org. Gen. Urin.*, 1891) were entirely unsuccessful. Krogius could not find the colon bacillus in a single one of the seventeen cases that he examined. And Melchior, although he found pathogenic germs in seven cases out of twelve (six of these were women), only discovered the bacillus coli once, and admits that possibly, even on this occasion, it may have been introduced by the bougie. There can be little doubt that though pathogenic organisms frequently enter the urethra, they seldom find a resting place in it, so long as it is healthy. The bulk of the organisms that inhabit the deep part of the male urethra are non-pathogenic.

When the urethra has been altered by stricture or by enlargement of the prostate the chances of pathogenic organisms being able to maintain themselves in it are much greater. The conditions are better suited to them. There is always behind an old stricture an irregularly shaped dilatation, with rigid walls, coated over with stagnant urine and mucus. And in some cases of enlargement of the prostate, the prostatic portion of the urethra is in nearly the same condition. Consequently, under these circumstances, pathogenic organisms are found not unfrequently.

I. Can the micro-organisms reach the bladder from the urethra of themselves, or must they be carried in ?

This depends upon the condition of the walls of the urethra. If they are inflamed it is a matter of common notoriety that infection can spread upwards into the bladder by direct continuity. Acute urethritis is a common cause for cystitis in both sexes.

If, on the other hand, the urethra is healthy, there is considerable difficulty, so far at least as the male sex is concerned.

In men the route to the bladder is well protected. The length of the passage; the close adaptation of its walls; the strength of the muscles around its membranous portion, and the rush of urine down it are tolerably efficient safeguards. Except in cases of enlargement of the prostate, spontaneous cystitis, that is to say inflammation of the bladder occurring without surgical interference or some other distinct and evident reason, is not common in men.

In cases of enlargement of the prostate spontaneous cystitis is fairly frequent. Inflammation of the bladder often occurs in them without an instrument having been passed. In all such in which I have examined the urine one of the organisms present has been the bacillus coli. The explanation is either that this organism can gain entrance to the bladder more easily under these conditions (perhaps from the rectum), or, as seems more probable, that the conditions are so favourable to its growth, that if it does by any accident gain the bladder, it never fails to cause septic decomposition of the urine and set up cystitis.

In women it is quite different. The urethra is short and wide. The muscles that guard the neck of the bladder are weak. The germs are present in profusion, and as a consequence, suppurative cystitis, originating without an apparent cause, is by no means unusual.

Inflammation of the bladder, for example, is not uncommon in women after severe operations that necessitate absolute rest in the recumbent position. The muscular strength of the bladder is not so great in women as it is in men. The recumbent position is a distinct disadvantage in the act of micturition. The bladder is not emptied. A certain amount of urine is habitually retained. Sooner or later the germs, which under these circumstances collect in even more than their usual abundance in the region of the meatus, find their way up the urethra, and set up cystitis. The partial retention of urine has given them their opportunity. As soon as the patient is allowed to sit up and empty the bladder thoroughly, the inflammation subsides of itself. I have often known the catheter blamed under these circumstances, and no doubt in a very large number of cases, deservedly. But cystitis such as I have described is by no means unusual in cases in which a catheter has never been passed.

The same explanation holds good for the slight attacks of cystitis that sometimes occur in women during the menstrual period. There is no retention of urine, it is true. The place of the retention is taken by the congestion that affects the bladder at that time, in common with all the other pelvic organs. This is the accessory cause. The pyogenic organisms find their way in without difficulty, and suppurative cystitis follows. When the congestion disappears at the end of the menstrual period the cystitis disappears with it ; the germs have no further hold.

In a very large number of instances, both in men and women, when the bladder becomes infected through the urethra, a catheter or some other instrument is the immediate agent.

The clinical proof of this is overwhelming. Retention of urine arises from various causes. It may be the result of shock, or of injury to the spinal cord, or of some mechanical obstruction, such as stricture or enlargement of the prostate. If not relieved, it leads to incontinence of urine (so-called), atony of the bladder, or even worse results. But except in those cases in which inflammation is caused by direct extension, or by infection from the kidneys, cystitis does not begin until an instrument is passed. And the greater the care that is taken in the preparation and passing of the instrument, the longer the outbreak is delayed.

The introduction of pyogenic organisms by the catheter is by far the commonest cause. The catheter itself may not have been properly sterilised. It may have been sterilised and then touched with septic hands. It may have come into contact with the bed-clothes, or with the patient's garments. It may have picked up some micro-organisms from the skin of the glans penis or of the meatus. Or it may have swept some in from the deeper part of the urethra, though these, so long as the urethra is healthy, are for the most part non-pathogenic. Wherever they have come from, it is certain that pyogenic organisms have entered the bladder, and that their entrance is simultaneous with the introduction of the catheter.

Fortunately their presence alone is not enough. There must be some accessory cause, such as retention of urine, or congestion of the mucous membrane. In the absence of such accessory, the micro-organisms, no matter how numerous, do no harm. Were it otherwise, cystitis would always follow catheterism, as it is usually practised.

II. Pyogenic organisms may enter the bladder with the urine, passing down the ureters from the kidneys. The effect is the same, whatever the mode of entrance. If the bladder is healthy and empties itself thoroughly, the micro-organisms do no harm. I have known many cases of pyonephrosis in which myriads of bacteria have passed through the bladder for weeks together, without causing the least trace of inflammation. If, however, there is retention of urine, partial or complete, or if the neck of the bladder becomes congested from any cause, cystitis follows at once.

The frequency with which the bladder is infected by this route is very difficult to estimate. Suppurative cystitis often occurs in old men with enlargement of the prostate, without an instrument having been passed. The organism present in these cases is nearly always the bacillus coli. It was so in all the cases that I examined, whose urine was acid. Now for infection to take place by this route, the bacillus must first get into the circulation, and then it must be excreted by the kidneys. Once in the urine there is no difficulty in understanding how it acts, for in these cases there is always residual urine.

There is little or no difficulty in the first of these steps. The bacillus can get into the circulation from the alimentary canal at almost any time. It exists in abundance in the intestines, and although it may experience some difficulty in traversing the intestinal wall during health, there is little doubt that it can do so in patients who are suffering from the slightest intestinal trouble, even an attack of constipation.

It has been definitely proved that the bacillus coli and the bacillus prodigiosus are able to pass through the walls of the intestines in rabbits under these conditions. Posner and Lewin (*Berl. Klin. Woch.*, 1895, no. 6) have shown, that if intestinal obstruction is produced in these animals by ligaturing the intestine, and a culture of either of these bacilli is injected into the bowel, in a few hours' time they can be found in abundance in the blood and in the urine. This of course does not prove that they can traverse the wall of the human intestine, the mucous membrane of which is much thicker; but as the bacillus coli is frequently present in the pus of abscesses that lie near, but have never had any direct communication with, the bowel, it must be regarded as, at least, highly probable.

Melchior considers the transit as easy, and suggests that when the conditions are favourable, the bacillus coli is not only able to pass out of the intestine into the blood stream, but is able to pass back again from the blood into the bowel. If injected into the blood the bacillus coli disappears rapidly; and as it does not always make its appearance in the urine he suggests that it may be excreted, in part at least, by the intestine.

Reblaub ("Pyelonéphrite des Femmes Enceintes," *Arch. des Mal. des Org. Gen. Urin.*, 1892, p. 406) has shown that pyelonephritis can be caused by infection from the intestine in this way. He quotes five cases occurring in the course of pregnancy in which the pelvis of the kidney became inflamed. There was no cystitis, so that the bacillus could not have ascended from the bladder. His explanation is that the uterus compressed the ureter, causing a certain degree of renal retention; that owing to intercurrent intestinal troubles, the bacillus was enabled to traverse the wall and enter the blood-stream; and that when it was carried round to the kidney in the course of the circulation, it immediately seized upon the retained urine in the pelvis, in the same way that it would have seized upon residual urine in the bladder in a case of enlarged prostate, and set up purulent pyelitis.

In rabbits it is undoubtedly true that pyelitis can be produced like this. If one of the ureters is tied and a day or two afterwards a culture of the bacillus coli injected into the auricular vein, it follows with certainty. And according to Bazy (*Ann. des Mal. des Org. Gen. Urin.*, 1893, p. 815) the same thing is true of cystitis, if a ligature is placed around the penis, so as maintain retention of urine for six hours.

Unilateral pyonephrosis, due to the bacillus coli and quite independent of cystitis, is certainly not uncommon in pregnancy. The cases usually terminate well, for as soon as the cause disappears and the passage of the urine down the ureter becomes free again, the renal retention subsides, and with it the accessory cause that enabled the bacillus to take hold. I have had several such under my care, but I am not prepared to assert that this was the route followed by the bacillus in all of them. Infection may take place, sometimes at least, through the lymphatic system. The kidneys are in close relation with the colon; and if in consequence of constipation or any other intestinal trouble, the bacillus is once enabled to pass the epithelial barrier, it can probably find its way almost as readily through the interstices of the tissues, directly into the kidney, as indirectly through the blood-stream.

Whether the bacillus, when it has once gained the blood-stream passes into the urine through the kidney seems to depend on the condition of that organ. The germs of many of the specific diseases, as well as pyogenic organisms have, as I have already mentioned, been often found in the urine. But it seems probable that they are never excreted in this way unless there is some renal lesion, though not necessarily of a very serious character.

Pernice and Scagliosi, for example (*Riforma Medica*, nos. 97, 98, 1892), injected known quantities of pure cultures of staphylococci, micrococcus prodigiosus, bacillus subtilis, and other organisms, into the blood of dogs, guinea-pigs and rats, and found them later in the urine. But there was in nearly all distinct evidence of acute inflammation of the glomeruli. Wyssokowicz (*Zeit. für Hyg.*, vol. i., p. 3, 1886) following the same method, but making plate cultures from the urine, found that the result depended upon the kind of organism. If it was of a kind that did not affect the kidney, it never appeared in the urine. If on the other hand, it did affect the kidney, it made its appearance thirteen times out of seventeen. Micro-organisms are only excreted by the kidney, when the blood that contains them escapes into the uriniferous tubules as the result either of injury or of inflammation. Sherrington, too (*Journal of Path. and Bact.*, 1893, vol. i., p. 258), arrived at the same result. Hæmoglobin was always present in the urine when micro-organisms were excreted by the kidneys.

So far as patients who suffer from enlarged prostate are concerned (and they are the ones in whom what is called spontaneous cystitis is most prone to occur) this point is not of very great importance. Renal degeneration is so common in them that it almost appears to be the rule, in those at any rate, in whom residual urine is habitually present. If the bacillus once enters the blood-stream in them it can easily pass into the urine and be carried down into the bladder.

III. The mucous membrane of the bladder may be infected directly through the agency of the capillaries. Infective emboli may be carried to it by the blood in the course of some general disorder. But so far as the bladder is concerned, this is so rare, apart from tuberculous disease, that I shall leave it to be dealt with later, when that subject comes up for consideration.

IV. Pyogenic organisms may gain access to the wall of the bladder through the medium of the lymphatics, and, provided other conditions are suitable, may set up cystitis.

The most direct evidence on this point is experimental, and it is fairly conclusive.

In male rabbits, inflammation of the bladder can be caused by extension through the walls of the neighbouring part of the bowel (Wreden, *Central. f. Chirurgie*, 1893, no. 27, p. 578). If the epithelium of the rectum is injured by the injection of hot water, or by the application of croton oil, and a culture is injected into the bowel, the same organisms make their appearance in the urine, and if the necessary conditions are present (retention, for instance), cystitis follows. Even oil, if it is injected into the rectum after this has been denuded of its epithelial lining, finds its way into the bladder. But this never happens unless the seat of the lesion is on a level with, or a little above the prostate. If the lesion is below, it has no effect.

This is probably the explanation of those cases of cystitis that are occasionally met with after operations upon the lower part of the bowel. The shock of the operation causes temporary retention of urine, and the micro-organisms find their way in through the contiguous portion of the walls.

Nor is this true of the rectum only. Infective organisms may invade the bladder from other quarters and if the conditions are favourable, set up suppurative cystitis. This is more common in women than it is in men, owing to the frequency with which salpingitis and endometritis occur in them. But it may happen in both by direct extension from the small intestine, or from abscesses in the neighbourhood of the bladder.

The experiments performed by Reymond (*Ann. des Mal. des Org. Gen. Urin.*, May, 1893) are conclusive as to this. Injections of various kinds of organisms were made in the neighbourhood of the bladder in dogs and rabbits. Some were intra-peritoneal, others into the sub-peritoneal tissue. Invariably, if the penis was tied, so as to cause retention of urine, suppurative cystitis followed in the course of a few hours, and, whatever organism had been injected, the same was found in the urine. As Reymond points out, the cystitis in all these cases is local first, the inflammatory focus on the mucous surface corresponding in locality to the suppuration outside, and then later, when the urine is infected, becomes general.

THE TREATMENT OF SUPPURATIVE CYSTITIS.

Suppurative cystitis is due to the action of septic organisms. Of these organisms, the most common, and one of the most active, is the bacillus coli, one of the ordinary inhabitants of the large intestine. This bacillus sometimes gains access to the bladder through the urethra, sometimes through the blood-stream, and sometimes through the lymphatics. By itself, with nothing to help it, it is harmless, or almost harmless, so long as the tissues are healthy. To produce any effect it must either be an especially virulent growth, or it must be assisted by some other agent, such as the presence of other organisms, or of some morbid condition of the bladder. If these facts are borne in mind, it is evident that a good deal may be done in the way of preventing cystitis by clearing out the localities that harbour the organism, doing away with the conditions that favour its growth, and preventing its being carried into the bladder.

PROPHYLAXIS.

I. The localities which the bacillus coli chiefly frequents must be kept as clear as possible. Ordinarily speaking this organism is a harmless saprophyte. When the conditions are favourable to it, it may develop into an intensely infective agent.

There can be no doubt as to the evil influence of intestinal obstruction, and, to a less extent, of constipation. Clinical experience and experiments upon animals alike show that these conditions greatly increase the activity of the micro-organisms that inhabit the intestine. Not only is a larger amount of their toxic products retained and absorbed, but the organisms themselves become more virulent and better enabled to traverse the intestinal wall.

Diarrhœa, and disorders in which the intestinal contents undergo putrefactive decomposition are no less important in this respect. I attribute the fatal issue, in a case of septic infection that followed removal of a small polypoid outgrowth from the neck of the bladder, to the fact that the organism harboured in the intestine at the time was an especially virulent form of this bacillus. It has been demonstrated by experiments that the activity of the bacillus coli from a case of diarrhœa is much greater than that of a similar culture from healthy intestine, and infinitely less than that of one from a case of English cholera.

The greatest care therefore must be taken in every operation upon the urethra or the bladder, and in every case in which cystitis is likely to occur, to keep the intestinal tract throughout in as pure a condition as it is possible for it to be. Whether this is to be done by means of purgatives, or by what are commonly called intestinal antiseptics, or by both, must be determined at the time for each case. I am far from disparaging the use of intestinal antiesptics. Many of them, as I shall show later, have great influence, not only upon the contents of the intestine, but upon the character of the urine. So far, however, as this special indication is concerned, I do not consider that, in the case of operations, the action of any one of them is equal to that of purgatives, and especially calomel.

Equal attention must be paid to any other haunts of septic or pyogenic organisms that may be present in the neighbourhood of the bladder, such, for example, as are not uncommon in connection with the female generative organs. The fact that the micro-organisms that occur in the urine in cystitis are in so many instances identical with those that are present in the discharges from neighbouring organs, (as, for example, in many of the cases recorded by Bumm and Schnitzler), is sufficient to show how closely the one is dependent upon the other. It is scarcely possible to prevent the occurrence of cystitis, if suppuration is allowed to continue in the neighbourhood of a bladder that is not able to empty itself completely, or is liable to constant attacks of congestion.

Many of the cases of persistent cystitis that occur in women in, and after, middle life, are due to constant re-infection. Sometimes this takes place through the wall of the bladder by direct extension, as, for instance, in cases of pyosalpinx and endometritis. Sometimes it takes place through the urethra. The mucous membrane becomes congested, in sympathy with the hyperæmia of neighbouring organs; the urethral canal is short and wide; the muscles that guard it are relaxed and flaccid; and the micro-organisms that abound near its orifice, find little or no difficulty in entering. Whether infection takes place directly or indirectly, it is hopeless trying to effect a cure until the source has been removed.

II. After pyogenic organisms have entered the bladder a good deal may still be done to prevent them exercising their power. Unless they are surrounded by conditions that favour them, they can do nothing. And if in the course of an attack of cystitis the conditions cease to favour them, the inflammation soon begins to subside.

The most important of these conditions are retention of urine, partial or complete, and congestion of the walls of the bladder. The former supplies the organisms with a nutrient medium that suits them to perfection. The latter impairs the protective power of the vesical epithelium, and weakens the resistance of the tissues that lie beneath.

Retention of urine may be caused either by an increase in the resistance at the exit, as in cases of stricture, and many of enlargement of the prostate, or by weakness in the expulsive power of the bladder, or by both together.

The steps that should be taken to relieve it are beyond the scope of the present work. Strictures must be divided or dilated. Enlargement of the prostate must be removed, or means must be taken to evade the obstruction by means of catheters ; and other measures, suitable to each case, must be adopted as required. Whatever the cause, arrangements must be made by which the bladder can be emptied effectually, at least once in the twenty-four hours. If this is not done, and urine is allowed to remain habitually in the bladder, there is constant danger of cystitis. If the micro-organisms can only gain an entrance, inflammation is sure to follow.

Nor is congestion of the mucous membrane of less importance. It does not matter whether it is active or passive ; whether it is caused by an irritant such as cantharides or a calculus ; or whether it is the result of exposure to cold or of constant straining. The protective power of the epithelium is lost or greatly impaired, and any micro-organisms that find their way into the urine can invade the wall at once. As I have already mentioned the cystitis that is so frequent at the menstrual period, during the early stages of pregnancy, and when there is any displacement of, or large fibroid growth in the uterus, may be traced in great measure to this cause. And the same may be said of the inflammation that is so common in connection with enlargement of the prostate. The immediate cause undoubtedly is the entrance of pyogenic organisms. But these would be harmless were it not for the presence of residual urine and congestion.

III. Steps may be taken to prevent micro-organisms being carried into the bladder.

So far as the blood-vessels and lymphatics are concerned, little or nothing can be done. Germs that have managed to enter the circulation must be carried round to the kidneys in course of time; and then, some of them, will, in all probability, find their way into the bladder with the urine. Many must be destroyed en route. It has been shown by experiments that, if a certain quantity of germs which are known to possess the power of passing through the kidney, are injected into the circulation, the proportion that can be collected from the urine is a very small one. But no means other than maintaining the general health in the best possible condition are known by which this proportion can be further reduced.

Nor is it possible to do much more in the case of the urethra. It is not possible to increase the resistance that it offers to the ascent of micro-organisms along its mucous surface ; and therefore, in the female sex at least, cystitis must always be of common occurrence. The anatomical arrangements of the male urethra provide a much more efficient protection for the bladder.

On the other hand, a large proportion of cases of cystitis are caused by organisms being carried directly into the bladder by means of instruments, such as sounds and catheters, and injections. And a very great deal may be done to check this.

It is self-evident that the bladder must possess an extraordinary faculty for resisting or getting rid of septic organisms. In catheterism, as it is ordinarily practised, septic organisms are always being carried into the bladder. I have obtained the greatest variety of cultures from catheters, and I cannot call to mind ever having found one sterile, unless it had been thoroughly prepared beforehand. Yet so long as there is no retention of urine, or congestion of the mucous membrane, inflammation seldom occurs. It is not until one or other of these condition is present, or until the nervous control over the bladder is lost, as it is for example, in fracture of the spine, that cystitis follows. The frequency with which it occurs when these conditions are present, and the difficulty that there is in preventing it, may be taken as giving some idea of the frequency with which organisms are carried in. Catheters, unless special precautions are taken, are always septic.

Catheters should be made so that they can be cleaned and sterilised as easily and as thoroughly as any other surgical instruments. There must be no recesses or inequalities left to harbour germs or urine. Whatever the material of which the instrument is made, the surface, inside as well as out, should be perfectly smooth and even. It is not uncommon to see the outer surface highly finished, while the interior, the part that is most difficult to clean and which comes into closest contact with the urine, is left so rough and irregular that it is impossible to keep it aseptic. Nothing more foul can be imagined than the interior of an ordinary gum-elastic catheter that has been in use for a few weeks, and has been cleaned in the ordinary perfunctory manner.

The eye must be perfectly smooth, with rounded edges, slightly sunken below the surface. The end beyond the eye must be solid, so that it cannot act as a receptacle for urine. And the material of which the instrument is made must be capable of standing thorough sterilization without injury.

Metal and rubber instruments present little or no difficulty. They can be steamed or immersed in carbolic acid, or other disinfectants, of sufficient strength for a sufficient length of time to destroy any germs that adhere to them. Ordinary gum-elastic catheters, on the other hand, such as patients obtain for themselves require special care. Most disinfectants destroy the surface and render them useless in a very short time.

Sterilisation is almost impossible if a lubricant containing any kind of grease, such as oil or vaselin, is used. No antiseptic of reasonable strength can penetrate through this, and soda is quite inadmissible. Even if the catheter is thoroughly washed with hot soap and water, some of the grease is certain to have penetrated into the interior through the eye and to escape. The lubricant should always be a soluble one. For some time past I have employed either boroglyceride or lanolin which has been sterilised and which is kept aseptic by the addition of carbolic or boracic acid. I prefer these to pure sterilised glycerin, and to Guyon's preparations, which consist of equal parts of soap, water and glycerin, with carbolic acid, β-naphthol, or resorcin. The quantity prepared at any one time should be small, and it should be kept in a long, narrow, well-stoppered bottle.

The principles on which sterilisation should be carried out are easily laid down. The details, on the other hand, must vary in every case. And it must not be forgotten that the actual work must be entrusted, in many instances, either to nurses, or to the patients themselves, who often do not understand the importance of what they are wished to do, and still more often cannot wait to do it. One of the most difficult things is to induce them to provide themselves with a sufficient number of catheters, and to get rid of old ones. It often happens that because one instrument passes a little more easily than another, it is used to the exclusion of the rest, and is kept long after it is worn out, and pointed to with very mistaken pride.

The simplest method is to keep the catheter in an antiseptic liquid; but the difficulty is to find one that does not destroy the instrument. Guyon, moreover, has shown that there is another objection. If catheters are allowed to soak in an antiseptic for any length of time, so much is absorbed by the material that the surface becomes very irritating to the mucous membrane of the urethra.

Boracic acid is the least injurious. I have kept the aseptic catheters made for me by Messrs. Maw, Son and Thompson, immersed in a saturated solution for a month at a time, without the slightest change. But the antiseptic power of boracic acid is very small. Germs may not be able to grow in it, but it will not kill them.

Nitrate of silver (one part in a thousand) and corrosive sublimate (of the same strength) are much more efficacious; and well made catheters withstand their action for a considerable time. Fifteen minutes' immersion is sufficient in the case of the former. The latter requires rather longer. Barlow (*Archiv. f. Dermat. u. Syph.*, 1893) recommends that each catheter, before being used, should be washed through three times with the nitrate of silver solution; then left soaking in it for twenty minutes, and finally washed out with a saturated solution of boracic acid and lubricated with sterilised glycerin. And the same process, only in inverse order, is to be carried out again as soon as the instrument is withdrawn. The methods adopted by Albarran and Guyon are almost the same.

Where large numbers of catheters have to be dealt with at a time, sterilisation can be accomplished more satisfactorily by means of sulphurous acid gas. This method possesses the advantage that the instruments, after having been sterilised, need not be touched or removed. They can remain free from the risk of contamination until they are required for use. But on a small scale, and in private, disinfection by gases is difficult to carry out.

Disinfection by dry heat is most effectual, but requires the greatest care. Disinfection by steaming, in the apparatus recommended by Ward Cousins, or by boiling, can generally be managed without much difficulty. I always recommend patients who suffer from retention of urine, in connection with enlargement of the prostate, and who have to pass catheters upon themselves at frequent intervals, to keep two of Nicoll's glass catheter cases, with rubber tops and metal caps, suspended vertically in their wardrobe, or wherever it may be convenient. One of these is filled with boracic acid lotion, which should be renewed each day; the other is empty, except for a plug of absorbent carbolised cotton-wool at the bottom. Side by side with these is an ordinary glass irrigator, filled with a strong solution of extract of soap, and fitted with an india-rubber tube and stop-cock. Each catheter, as soon as possible after it has been used, is thoroughly washed out with the extract of soap, rinsed inside and out with hot water, if it is available, and dropped vertically into the tube filled with boracic acid. Once a day, or more frequently if it is necessary, all the catheters are taken out, boiled for five minutes, and placed to drain in the other Nicoll's case, where they remain until they are required.

Each patient should provide himself with a sufficient number of catheters, at least equal to the number of times that the urine has to be drawn off in the course of the twenty-four hours.

In this plan the catheters are not dried, which is, I admit, a defect. If thoroughly dried they undoubtedly last longer. But they are, as I have proved to my own satisfaction, sterilised sufficiently for all practical purposes, and after sterilisation they are kept free from the risk of contamination. The aseptic catheters, made for me by Messrs. Maw, Son & Thompson, are not affected in the least by boiling, if they are kept straight. If bent up, the varnish cracks upon the convexity and they are spoiled.

Guyon's method of disinfection by formalin vapour is simpler still. The catheters are thoroughly cleansed with soap and water, dried, and then placed side by side, in a long tin box, fitted with shelves inside, and closed with an expanding rubber lid. Running down one side of the box and separated from the catheters by a perforated partition, is a layer of cloth, thoroughly sprinkled with formalin. The vapour rising from this diffuses itself through the box and disinfects the catheters in the course of twenty-four hours. They may be kept in this way for almost any length of time without sustaining any injury; but the method is not suitable to small catheters with a fine bore; and the formalin vapour that adheres to the surface should be washed off with boracic acid before the catheter is used.

Nicoll's catheter cases, fitted with an inner tube of perforated metal, answer equally well, the cloth sprinkled with formalin occupying the space between the two tubes.

It is easy to lay down much more elaborate precautions ; but, according to my experience, it is very difficult to get the simplest carried out thoroughly, especially when a catheter is required at night, or many times during the day.

Sounds should be substituted for catheters wherever it is possible, as they are so much more safe. If stilets are needed, they should be plated, and kept separately from the catheters, or they are certain to rust and spoil the instument.

Sterilisation of the catheter alone is not sufficient. The urethra itself is full of germs, some of which at least are likely to be carried in by the catheter. Lustgarten and Mannaberg (*Vierteljahr. f. Derm. u. Syph.*, 1887), found that there were numbers of them in the urethra, even when the mucous membrane was perfectly normal. Rovsing (*Die Blasenentz*, Berlin, 1890) found them in 22 cases out of 30. And although, according to Petit and Wasserman, the majority of those inhabiting the urethra are non-pathogenic, the bacillus coli has been found there by Bouchard (*Soc. de Biologie*, 1890) and by Melchior. It must be admitted at once, however, that disinfection of the urethra as a routine method, is impracticable; patients will never carry it out.

Whether it can be carried out under any circumstances is questionable. Petit and Wasserman, using large quantities of a 4% solution of boracic acid, entirely failed. And although Barlow succeeded occasionally in rendering the mucous surface aseptic by means of a solution of nitrate of silver (one part in a thousand) he met with many failures.

It is as much as can be expected in actual practice, if the hands, the glans penis, the prepuce, and especially the lips of the meatus, are thoroughly washed with warm soap and water, and then well sponged over with nitrate of silver or corrosive sublimate, before the instrument is passed. Barlow (*loc. cit.*) is inclined to believe that the organisms which are swept along the urethra by the catheter, are for the most part prevented from passing into the bladder by the action of the muscles that surround the membranous portion; and that when infection of the urine in the bladder is caused by the catheter, the germs are either in the eye, or in the interior of the instrument, or else have been dried on to its outer surface too firmly to be removed in this way.

In cases in which the protection of the bladder is of very great importance, as, for example, when residual urine has to be drawn off at the beginning of catheter life, and those instances in which the urethra is already inflamed, and therefore full of germs, it is advisable to make use of Melchior's catheter, so that the part of the instument that enters the bladder may never have been in contact with the urethra. The only alternative is to inject into the bladder, after it has been thoroughly emptied, half an ounce of a 2% solution of nitrate of silver, with the view of preventing the growth of any organisms that may have been carried in.

GENERAL TREATMENT.

The general principles upon which the treatment of suppurative cystitis should be carried out, scarcely need be stated. Causes must be removed as far and as speedily as they can be: meanwhile, symptoms must be relieved.

The causes of suppurative cystitis are always local. The chief treatment, therefore, must be local. Many of the symptoms, however, admit of relief, if not of cure, by means of constitutional remedies.

In all but trivial cases the patient should be confined to bed, with the hips raised as far as is consistent with comfort; and the room kept at an even temperature. Like the kidneys, the bladder is very susceptible to the influence of cold, especially when it is inflamed. The mucous membrane at the neck becomes congested and swollen, and if there is the least obstruction at the exit, such, for example, as is common in cases of enlargement of the prostate, retention of urine follows.

Hot baths, at a temperature of 100° to 105° F., for fifteen or twenty minutes, give the greatest relief; and if the action of the heart is good, and care is taken to avoid a chill afterwards, may be ordered night and morning, or even three times a day in acute cases. Poultices and hot fomentations are a very poor substitute. Hot enemata are strongly recommended by some; but unless an action of the bowels is considered advisable, the discomfort more than counterbalances the relief. If much throbbing is complained of in the perineum, a few leeches may be applied behind the scrotum, but they are rarely required unless the prostatic portion of the urethra or the periprostatic tissues are affected as well as the bladder.

The diet must be light and unstimulating. In acute cases, occurring in young subjects, I have often found great advantage from restricting it to milk and soda water for a few days. Most patients are better without meat, or with a very small quantity. Fresh fruit may generally be allowed freely. In fact, great credit is given by some to decoctions made from fresh blackberries or raspberries. Asparagus, rhubarb, tomatoes, and vegetables generally that contain lime salts, should be avoided. Rich food of any kind is distinctly injurious.

Alcohol is not advisable in cystitis, unless the condition of the circulation is such as to require it, or the patient is unable to digest his food, or to sleep without it. It increases the amount of work to be done by the bladder; renders the urine more irritating, weakens the nervous mechanism that presides over micturition, and makes the patient more susceptible to changes in temperature. In any case sherry, champagne, and beer should be avoided. Light claret, old port, or a little old whiskey or gin may be taken if required, but always, as far as possible, with food.

No restriction should be placed upon the amount of fluid taken. Many patients stint themselves in this respect under the mistaken notion that it will give the bladder less work to do. The benefit derived from the decoctions of triticum repens, mallow, linseed and many other substances that have been recommended for cystitis, is probably due more to the quantity of fluid taken, than anything else. There is at least no proof that their demulcent properties extend beyond the alimentary canal. Alkaline mineral waters may be allowed freely, especially in those cases in which the urine is very acid, and inclined to deposit crystals of uric acid. Hard water is injurious.

The bowels should be opened at once, preferably by means of a mercurial purge, and then kept freely open. It is true that, under normal conditions, the vesical and prostatic veins do not empty themselves to any material extent into the hæmorrhoidal plexus ; but there can be no question, especially in old men, that constipation and straining at stool very greatly increase the tendency to vesical congestion. Further, as I have already pointed out, when the bowels are confined, the number of organisms in the intestines and the amount of poisonous substances they produce for subsequent absorption, are both greatly increased.

When the urine is highly acid, and especially when there is a tendency to the deposit of uric acid crystals, alkalies, such as the bicarbonate and citrate of soda and potash, are of service in allaying irritation ; or the liquor potassæ may be given in barley water, well diluted ; but it is a mistake to give alkalies as a routine treatment in cystitis. Where the urine is alkaline already, they only do harm. If the alkalinity is due to ammonia, antiseptics are required. If to a fixed alkali, boracic acid and benzoate of soda are most effectual so far as the urine is concerned. Care, however, must be taken not to cause dyspepsia ; and it must always be remembered that persistently alkaline urine is strongly suggestive of the existence of some grave disorder of nutrition.

Acute cystitis is always attended by a certain degree of fever ; but unless the exit from the bladder is obstructed, or the prostate, or the perivesical cellular tissue is involved, the temperature seldom rises very high. In ordinary cases there is but little absorption from the bladder. Antipyretics, therefore, are rarely required as such, although both antipyrin and quinine are of value, owing to their power as antiseptics when excreted by the kidneys.

Opium is the only drug that can be relied upon to give relief when strangury is severe. Full doses are required, particularly in young subjects. Caution must be exercised in the case of older patients with cystitis of long standing, or if there is any reason to suspect that the condition of the kidneys is not satisfactory. It may be given by the mouth, or preferably, by the rectum, in the form of a suppository. I do not consider it advisable to inject morphia into the bladder. As a rule it is not absorbed, and does no good. Every now and then (probably when there is a recent abrasion or denudation of the surface) it is absorbed much too quickly. Opium often seems to act better when combined with belladonna or henbane, both of which have some influence in diminishing the irritability of the bladder.

Cocain, which is so excellent for the urethra, is of little use when the neck of the bladder is concerned. Moreover, when it is injected into the bladder or the prostatic portion of the urethra, it has the grave drawback of increasing the congestion of the mucous membrane. Attacks of hæmorrhage, and even of retention of urine, may occur from this cause, if cocain is used in patients suffering from enlargement of the prostate. In the intense strangury that is so common in connection with tubercular cystitis, it scarcely gives a moment's relief.

Guyon recommends an injection of a 10% solution of antipyrin in those cases in which burning pain at the neck of the bladder persists after the application of nitrate of silver or corrosive sublimate. Its action is much more slow than that of cocain or morphia. Guaiacol (5% dissolved in sterilised olive oil) sometimes relieves the pain of tubercular cystitis very considerably.

Bromide of sodium and ammonium and chloral are chiefly of service in those cases in which there is general irritability of the nervous system, and opium or morphia is inadmissible. Sulphonal and paraldehyde may be given when sleeplessness is a troublesome symptom ; but they have little or no effect upon strangury.

After the acute stage of cystitis has subsided, and there is no longer pain, or great increase in the frequency of micturition, but merely a purulent cloud in the urine, coming from the swollen and congested mucous membrane, more benefit is obtained from the administration of resins, such as turpentine, copaiba, sandal wood oil, and sanmetto. The effect they produce is due, in great measure, to the fact that they are excreted by the mucous membrane that lines the urinary organs. In all probability the reputation enjoyed by buchu and uvæ ursi is to be attributed to the small quantities of oleoresinous substances that they contain. They are chiefly of use as diluents.

Freudenburg (*Wiener Klin. Woch.*, June 6th, 1895) recommends minute doses of cantharidin, dissolved in alcohol, in the same class of case. I have found it beneficial when a slight degree of strangury obstinately persists in a young adult, without any apparent cause. But when the strangury is associated with enlargement of the prostate and passive congestion of the mucous membrane at the neck of the bladder, I believe it does more harm than good. Certainly it aggravates the symptoms for a time, though there may be some improvement afterwards.

A great deal has been expected from the action of intestinal antiseptics in suppurative cystitis; but the results, so far as the direct effect upon the urine is concerned, have not been commensurate. The intestinal canal can be disinfected, by naphthalin for example, so that the fæces are almost odourless; and a certain amount of naphthalin is absorbed and excreted at length by the kidneys. But it never appears to be sufficient to exert any real antiseptic power upon the urine. I have experimented very largely with this class of drug, and although there is no doubt that the composition of the urine can be modified, so that it is less favourable to the growth of organisms, I do not think it is possible to introduce a sufficient quantity of the antiseptic to do more. The drugs themselves in many instances are only sparingly soluble, and in others are distinctly irritating in character. The patients, only too often, are broken down in health, with more or less renal degeneration; and great care has to be exercised not to cause an attack of dyspepsia.

Indirectly, however, and associated with purgatives, such as calomel, these drugs may be of the greatest service. One of the main sources whence the bacillus coli spreads to the urinary organs can be cleared out, and the formation of toxins, which might be absorbed and act very deleteriously upon the health, can be almost entirely stopped.

Quinine and antipyrin have both of them a certain influence upon the urine. They are rarely given, however, with this object in view as they are, neither of them, even when given in excessive doses, capable of preventing the growth of organisms in the urine.

Salol given in cachets, in two or three grain doses, five or six times a day, is the antiseptic that I have found the most satisfactory. Unfortunately it is very insoluble. In several instances it has formed intestinal concretions, probably as Dr. Marshall has shown, owing to the fact that its melting point is little, if at all, above the temperature of the intestinal tract during digestion. The salol melts, forms a fluid that does not mix readily with the food, and then, as digestion comes to an end, crystallizes again, in the form of a more or less solid mass. In one case recorded by Brossard, a calculus weighing as much as four grammes, and composed almost entirely of recrystallised salol, was passed. There is no doubt, however, as to the effect that it exerts upon the urine; and though I have given it in a very large number of cases, I have never, myself, known any inconvenience caused by it. This may be due to the fact that when given in small doses at frequent intervals, there is less chance of any accumulation taking place.

Benzonaphthol, a tasteless and odourless powder that passes through the stomach without change, and breaks up in the intestine in β-naphthol and benzoic acid; and betol, which, in a similar way, is decomposed into β-naphthol and salicylic acid, are of use in cases in which the urine is offensive. They check the formation of indol, one of the products of the bacillus coli, as shown not only by the diminution in the odour of the fæces, but by the diminished amount of indoxyl in the urine; and they render the urine less liable to decompose when exposed to the air or infected by a culture.

The former of the two, benzonaphthol, is especially indicated when the urine is alkaline from the presence in excess of a fixed alkali. They may be given in cachets, in five to eight grain doses, three times a day. Neither of them is easily soluble in water.

Naphthalin (gr. ii. to gr. iv. in the form of a pill) and hydroquinone (gr. iv. to viii.) have also been recommended, the former for its action upon the bacillus of typhoid, and therefore probably upon the bacillus coli: the latter for the rapidity with which it passes into the urine. The sulpho-carbolate of soda which, some time ago, I tried largely in fifteen-grain doses, I was disappointed with, so far as the urine is concerned, although it appears to possess considerable antiseptic power over the upper part of the alimentary canal.

Benzoic acid and boric acid answer best when the urine is alkaline from the presence of a fixed alkali. The former may be given in the form of a pill, up to twenty grains a day; the latter in even larger doses. The benzoates of soda and ammonia are equally satisfactory, so far as the reaction of the urine is concerned, and interfere less with digestion. Their antiseptic power, however, is very slight.

Besides these, a large number of other drugs have been recommended from time to time; but though they are occasionally of use, their reputation rests rather upon clinical reports, often of a very vague character, than upon direct proof. The best, perhaps, is the fluid extract of Collinsonia. This is undoubtedly beneficial in chronic cases, with atony of the muscular coat. Pichi (the extract of Fabiana imbricata); piperazin, diuretin and many more have been well spoken of, and in some cases I have known considerable benefit occur during their administration; but I do not consider it by any means certain that the improvement was the result of their action, and not of the other measures adopted at the same time.

LOCAL TREATMENT.

The first essential is to remove all accessory sources of irritation that may be present, such as calculi. Suppurative cystitis cannot be cured, so long as additional causes, such as these, are allowed to remain. The next is to destroy, remove, or starve out the septic organisms that have found their way in. So long as the pathogenic organisms are confined to the urine, and the walls of the bladder are not infected, this is comparatively simple. When, however, the mucous membrane is invaded, the difficulty becomes greater, and the subsequent condition less satisfactory.

If the bladder can empty itself thoroughly and satisfactorily, even if it is only once in the twenty-four hours, suppurative cystitis soon yields to treatment. The bladder clears itself. The organisms that are growing in the urine are swept away or destroyed; and, though much more slowly, the same fate overtakes those that have penetrated into the mucous membrane.

If the bladder cannot empty itself, either it must be emptied by artificial means; or the organisms must be destroyed *in situ;* or both must be done.

I. The bladder can be emptied and drained, either through the urethra, or through an artificial opening. In the former case, a catheter is passed at regular intervals, or is tied in. In the latter, an incision is made into the bladder supra pubes, or through the perineum or vagina, according to sex, and drainage maintained through a tube, for so long as it may be considered advisable.

Each case must be judged upon its own merits. It is manifestly impossible, considering the number of causes for cystitis that there are, and the still greater variety of patients, to lay down definite rules as to the particular method that is to be employed in each case, or the time when it is to be employed. I am, however, strongly of opinion that temporary drainage of the bladder through an artificial opening, giving it perfect rest for a time, might be adopted in cases of suppurative cystitis much more freely than it is at present, with great advantage.

Cystitis cannot last for any length of time without inflicting very grave injury upon the bladder and upon the kidneys. In some cases, the walls of the bladder become hard and rigid from organisation of the exudation that fills all the interstices between the tissues. In others, the muscular coat loses its power, so that the wall yields and stretches, and great pouches form. In either case the backward pressure soon affects the ureters and the pelvis of the kidneys. They become dilated; the renal cortex becomes atrophied; and chronic interstitial nephritis follows.

The longer the cystitis lasts, the greater the changes that it induces, and the more difficult it becomes to cure. Yet cases are often allowed to continue for years, partly because the inconvenience is not very grave at any one time, partly from an exaggerated idea of the risk that attends, and the inconvenience that follows such a simple proceeding as drainage of the bladder. I have never had occasion to regret having drained a bladder. I have often regretted that I did not do so at an earlier date.

When the attack is not very severe, or the symptoms urgent, the bladder should be emptied thoroughly once a day. The softest catheter that can be passed should be used, and of course, every precaution must be taken that no further supply of organisms is introduced.

In cases of longer duration, in which the time and the persistence of the symptoms render it evident that the infection is no longer confined to the urine, but has involved the wall as well, it is not sufficient to empty the bladder once or twice a day. It must be kept empty.

The simplest manner in which this can be done is by tying a catheter into the bladder. If the shape of the bladder is normal, and the muscular coat retains its tone, the pressure of the viscera will keep it empty, even when the patient is lying down.

This method of draining the bladder is very popular, especially in France, owing in great measure to the powerful advocacy of Guyon; and it has much to recommend it. It diminishes congestion, like everything else that empties the bladder. It protects the urethra (not quite perfectly) from absorbing any of the toxins that are produced by septic organisms in the urine. If the catheter is a flexible one, and it is not carried too far into the bladder, it causes exceedingly little inconvenience. The patient can even move about in his room. And if the eye is only just inside the bladder, it drains it fairly well. The urine should flow from the catheter drop by drop, without any break. If, when the catheter is moved either backwards or forwards, a small stream flows out, the eye of the catheter is in the wrong place, and the drainage is imperfect.

On the other hand, it has a great many drawbacks. It does not answer when there is a large flaccid bladder, or in cases in which there is a thin-walled post-prostatic pouch, and these are often the ones that need drainage most. The walls of the bladder collapse and fall together, instead of contracting uniformly towards the orifice, and the recesses remain undrained. Inflammation of the urethra is not uncommon if the catheter is kept in more than a day or two, even though the surface is perfectly smooth and it is changed sufficiently often ; and the inflammation may spread to the bladder itself, or to the epididymis, or to the veins that form the prostatic plexus. In other cases the kidneys resent it. I have known on several occasions suppression of urine caused by tying a catheter into the urethra, in women as well as in men ; and I have known it continue until the catheter was withdrawn. In short it is only in comparatively slight cases, in which the wall of the bladder is but little affected, and the kidneys are still sound, that this method of drainage can be regarded as safe or efficient. In those cases that need it most, it often fails to keep the bladder empty, and it is always attended by a considerable amount of risk.

The bladder may be drained with greater certainty through an artificial opening. This may be made either over the pubes, in the perineum, or (in the female sex) through the vesico-vaginal septum.

Supra-pubic drainage. At first sight an incision into the front wall of the bladder, over the pubes, appears to be very ill-adapted for drainage. The wound is of necessity a deep one. Owing to the looseness of the tissues between the bladder and the anterior abdominal wall and the movements of the bladder, there appears to be some risk of urinary infiltration; and the opening into the bladder is very far from being at the lowest part. On the other hand, it enables the whole cavity of the bladder to be explored, so that there is no chance of a calculus or other unsuspected irritant being overlooked. The patient after the first few days can sit down and move about with comfort. A post-prostatic pouch can be kept empty by means of a suitably curved india-rubber tube. Although the opening is not at the lowest point, the pressure of the viscera above and behind the bladder keeps it fairly empty, even when the patient is lying upon his back in bed; and unless the incision made into the bladder is of unusual length (as, for instance, when there is a large calculus to be extracted) the patient remains perfectly dry. If the opening has to be maintained permanently, or even for a considerable length of time, there can be no doubt as to the superiority of the supra-pubic over the other methods, in women as well as in men. Great care, however, must be exercised in performing this operation when the bladder is small and rigidly contracted.

The operation is performed with the usual precautions. The day before, the skin over the pubes is shaved, thoroughly well scrubbed with soap and water, and covered with a carbolic compress. At the time of the operation the bladder is emptied by means of a catheter, and well washed out with a warm solution of boracic acid. It is hopeless trying to disinfect the walls in a case of advanced cystitis requiring drainage, but care should be taken that the contents (some of which are sure to enter the supra-pubic space) are as little septic as possible. Sufficient is left in to fill the bladder to moderation. As a rule eight ounces are enough, but if the bladder is small and rigid, or there is any reason to suspect the presence of sacculi, this must be reduced by one-half. I have long since abandoned distension of the rectum. It tends, it is true, to raise and fix the floor of the bladder, but where the question is merely one of drainage, this is unnecessary, and it is not altogether devoid of danger.

Trendelenburg's position may be adopted with advantage, if the patient's respiration is good; but as the weight of the viscera presses upwards against the diaphragm, care is required in the cases of old men with rigid chests and emphysematous lungs.

The incision is in the middle line, from one and a half to two inches in length, according to the amount of fat to be traversed, and beginning over the symphysis. The tendinous structures are divided down to the anterior lamella of the transversalis fascia. As soon as this has been opened, the finger is introduced and the sub-peritoneal fat, peritoneum and fascia carefully lifted off the bladder wall and hooked upwards with the finger nail. If the bladder is tense and prominent, it may be punctured at once with a scalpel, avoiding the veins that run down the anterior wall, and the finger introduced behind the blade to hook up the wall. If, on the other hand, it is deeply situated, a tenaculum should be fixed in it to hold it more firmly.

If there is nothing that requires removal, there is no need to insert any sutures in the bladder wall. A soft rubber drainage tube should be introduced well into the cavity, and fixed there, either by means of a suture passed through the skin, or preferably by a plate that slides up and down upon the tube, and can be secured by strapping. The other end can be conducted to a vessel underneath the bed. The upper part of the incision can then be drawn together by a suture, and soft absorbent dressings applied.

In this way the patient can be kept perfectly dry; the bladder can be washed out as often as required, either through the urethra or through the tube; and at the end of three or four days when the soft tissues around the wound are consolidated, the tube can be removed and replaced or not, as may be wished.

Perineal drainage. There are several ways in which this may be carried out. The opening may be made at the apex of the prostate, so that the drainage tube is carried along the prostatic portion of the urethra and enters the bladder at the natural orifice. Or it may be made directly into the bladder, through the substance of the prostate. Or, as Howlett has suggested, it may pass, in certain cases, behind the prostate altogether, and enter the bladder near the base of the trigone.

Sir H. Thompson (*Diseases of the Prostate,* sixth edit., p. 178) recommends the first-named, as "on the whole, more useful and more generally available in most of the instances in which efficient surgical relief is demanded."

"I employ the central incision, using a median grooved staff, and a long straight narrow-bladed knife, with the back blunt to the point. Having placed the left index finger in the rectum, the knife may be introduced, edge upwards, about three quarters of an inch above the anus, with or without a small preliminary incision of the skin (I prefer the former) until the point reaches the staff about the apex of the prostate gland, where it divides the urethra for half-an-inch or so, and is then drawn out, cutting upwards a little in the act, but so as to avoid any material division of the bulb. The left index finger is now removed from the rectum, simply wiped upon a napkin, and following the groove of the staff, slowly pushed through the neck of the bladder as the staff is withdrawn." One of Annandale's rubber tubes should then be introduced, so that its extremity lies just within the bladder; or if the prostate is enlarged, one of Watson's; and the projecting end secured by a suture or a bandage.

I have tried this plan on many occasions in all forms of cystitis, with, in most, very great benefit. But I am inclined to believe that in those which are associated with any considerable degree of enlargement of the prostate, Harrison's method of tapping directly through the gland is to be preferred.

The patient is placed in the lithotomy position and the left forefinger introduced into the rectum to act as a guide. A straight trocar and cannula is then pushed through the middle line of the perineum, three quarters of an inch in front of the anus, through the enlarged portion of the prostate, straight into the bladder. The trocar is withdrawn, and the cannula secured with tapes in the ordinary fashion. When the patient wishes to get up a rubber tube can be fastened on to the end of the cannula, and the other end of the tube led off into a portable urinal, or secured by a clip. There is the further advantage that in a considerable number of cases this is followed by a definite reduction in size of the prostate, even if it is only due to the subsidence of congestion.

So long as the patient is confined to bed the perineal method of drainage answers every purpose. The bladder is emptied from its lowest point, and the tube can be easily arranged so that the bedclothes are not soiled. The discomfort, however, when the patient gets up is very great, much greater than it is when the bladder is drained supra pubes; and sitting down is even worse. For this reason I prefer the supra-pubic method unless it is certain that drainage will only be required for a few days.

Dilatation of the urethra, either digital or instrumental, which has proved of great service in spasmodic contraction of the neck of the bladder in women (Teale, *Lancet*, 1875) is of little use for drainage. Unless the dilatation is carried to a point that may entail permanent loss of power, the neck of the bladder soon recovers sufficiently to prevent some of the urine escaping; and drainage is of no use unless it is complete.

Dilatation of the female urethra, combined with division of the external orifice in the median posterior line, answers a little better; but even this does not compare in any way with an incision directly into the bladder, through the vesico-vaginal septum. This ensures complete rest. All the urine drains out through the opening. The bladder is left absolutely empty. There is no need to insert a tube, unless it is wished to keep the communication open for a considerable space of time. A simple median incision is sufficient. It is quite unattended by risk; and if left to itself, usually closes up in the course of three weeks or a month, without in any way endangering the patient's subsequent control over her bladder.

As to the length of time during which it is advisable to continue drainage, no rule can be laid down. If the cure is to be permanent it must be kept up until the congestion that accompanies, and in many cases precedes, the cystitis has completely disappeared; until the urine has regained its normal reaction, and is free, or almost free from pus; until the muscular coat has regained its tone; and until the walls of the bladder have had time to throw off the dense coating of phosphates that clings to them in so many of these cases, and free themselves from the accumulation of lymph that fills their interstices, and renders them hard and rigid. If the cystitis has lasted only a short time, a few days of perfect rest may suffice. In those cases in which the walls are thickened and unyielding, it may be many months before the inflammatory exudation is absorbed, and the muscular fibres regain their power of contraction and relaxation. Meanwhile, other measures must not be neglected, especially as it is not uncommon to find that treatment which was resented by the bladder, and appeared only to make matters worse before drainage was begun, succeeds as rapidly as could be wished when the bladder is placed thoroughly at rest.

II. Suppurative cystitis is due to septic organisms that have found their way into the bladder. If the bladder cannot get rid of them by its own action, steps must be taken to destroy them, or at least to check their growth by means of antiseptics. I have already shown how much can be done with these through the medium of the intestine and kidneys. It remains now to deal with their effect when applied locally.

There are two ways in which they are used.

The bladder may be washed out with a dilute antiseptic, using a considerable quantity of fluid; or what Guyon calls instillation may be tried. In this the bladder is emptied as thoroughly as possible, and a few drops of a much stronger solution are injected into the neck. Both those methods have their uses; and of course they may be combined with such internal remedies as are suitable to the case, or, if thought advisable, with drainage.

a. Washing out the bladder. The object in washing out the bladder is to get rid of the septic urine that stagnates in the recesses and between the folds; to cleanse the mucous membrane from the organisms and the urinary deposits that cling to it; to diminish the congested state of the blood vessels; and in some instances, by exciting tension, to apply a powerful stimulus to the muscular coat. No antiseptic that is not harmful can have any direct effect upon organisms that have already penetrated into the substance of the wall. But by freeing the surface of the epithelium from unhealthy urine and offensive deposits, the cells are given a chance of recovering themselves and regaining their defensive powers.

Washing out the bladder, if it is wished to be effectual, is by no means so simple a proceeding as it appears to be.

A full-sized metal catheter should be employed, with two eyes, and of as large a bore as possible. The bladder can be filled through the urethra without using a catheter at all, by employing about five feet of water pressure; but it cannot be washed out in this way. The catheter should be of metal, because it can be sterilised more easily, and because the current through a metal instrument is fuller and more rapid than that through a rubber or gum elastic one of the same outside measurement. And there should be two eyes, because when the fluid pours into the bladder through the catheter, it stirs up the stagnant urine more thoroughly if it comes from two directions than if it comes from one. A double current catheter does not answer the requirements at all.

Hydrostatic pressure, by means of a rubber tube attached to a glass container, is much better than a syringe. The current is more uniform and more easily graduated. A height of from two to three feet is usually sufficient, but this naturally depends upon the condition of the bladder and the amount of force lost in friction. And there should be a two-way vulcanite or metal tap attached to the catheter. Fluid that has once been in the bladder should not enter it again.

The liquid must enter rapidly and leave rapidly, so that there is no time for the deposit that has been stirred up to settle down again. The stream should be directed successively against different portions of the bladder wall. The floor naturally requires most attention. The quantity introduced at any one time depends upon the condition and the size of the bladder. Unless it is expressly intended, it should never be sufficient to fill the bladder, or to excite muscular contraction. Washing out the bladder should not cause tension or pain. It follows, therefore, that in acute cystitis, the bladder should not be washed out at all, unless there is some very urgent reason for it, and that in those cases of chronic cystitis in which the capacity is reduced, as I have known it, to two or three ounces, the quantity injected should be less still.

The urethra is infected in all cases of cystitis. It must, therefore, be washed out before the catheter is allowed to enter the bladder, though it is almost impossible to get it thoroughly aseptic. The meatus and the fossa navicularis are to be cleansed first. Then the catheter may be pushed on to the bulb, and the fluid allowed to stream back to the meatus. Meanwhile, the orifice of the urethra should be compressed once or twice around the shaft of the catheter, so as to distend the canal and ensure the complete unfolding of the mucous membrane. At the bulb there is often a dilatation capable of retaining half a drachm of fluid or even more. As soon as this has been thoroughly done, the catheter may be pushed on through the membranous part into the deep urethra.

Fluid that is injected into the prostatic portion of the urethra does not return by the side of the instrument like that injected into the anterior portion. Nor can it return through the catheter unless the prostatic portion of the urethra is dilated so as to form part of the bladder anatomically as well as physiologically. Unless, therefore, the level of the fluid in the reservoir is carefully watched, a considerable amount may be thrown into the bladder without its being perceived.

The temperature of the fluid in the reservoir should be two or three degrees above the normal, as it cools down considerably before it enters the bladder.

Fluid that is used to wash out the bladder must itself be aseptic. And it is advisable that it should be approximately of the same specific gravity as the urine. If the deficiency is great it can be made up in most instances by the addition of a sufficient quantity of sodium chloride, or of some other neutral salt that is inoffensive and does not cause any chemical reaction.

For purely cleansing purposes, sodium chloride and boric acid, dissolved in a solution of sodium borate, are the most useful. The former dissolves away the deposit of pus rather the more easily. The latter has some, though a very slight degree of antiseptic power. The sodium borate enables a rather larger amount of boric acid to be held in solution.

The best germicide, so far as the bladder is concerned, is nitrate of silver. The citrate of silver, which has been recently recommended as less irritating, is not so soluble.

The chloride that is formed almost at once is of course quite insoluble, but it appears to possess an exceptional faculty for preventing the growth of the bacillus coli. For washing out the bladder one per cent. is quite strong enough. This is more effectual than corrosive sublimate and less painful in suppurative cystitis. In tuberculous inflammation I have known a very weak solution of corrosive sublimate (1 in 20,000) borne better.

Iodine terchloride, (1 in 2000), I believe to be the next best. For all cases, however, in which there is evidence of passive congestion I prefer nitrate of silver.

Carbolic acid, of sufficient strength to act as an antiseptic, causes too much irritation. Quinine, boric acid, and naphthol check the growth of organisms, but so far at least as concerns the urine in the bladder, do not appear to possess the power of destroying them. Iodoform is of no use in suppurative cystitis; and nitric and phosphoric acids which have been recommended for the purpose of dissolving the concretions that form upon the wall, have little or no power under these conditions. If the organisms that cause the decomposition of urea are destroyed, the formation of the ammonio-magnesian phosphate ceases, and that which has been deposited already is thrown off by the epithelial cells as they are renewed from below. After orchidectomy in cases of enlargement of the prostate, I have many times noticed masses of phosphatic concretion that were previously firmly adherent to the mucous surface, separate themselves spontaneously as the wall recovered, and come away with the urine.

Sanitas, boro-glyceride, sulpho-carbolate of soda, salicylic acid, salicylate of soda, salts of bismuth and of lead, and many other substances have been recommended from time to time for washing out the bladder, and may occasionally be of use. Ichthyol and permanganate of potash deserve a certain amount of consideration. The former may be used in solution (half per cent. Villetti);

or as ichthyol ammonium (1 in 4000 Julius Fessler, *Archiv. f. Dermat. und Syph.*, 23, 1891, p. 355). It is said to be especially efficacious against the streptococcus and the gonococcus, causing a certain amount of desquamation of the surface, so that the cocci which have penetrated into or between the epithelial cells are carried away. I have had no experience of it. Permanganate of potash I have tried many times. In very dilute solution (1 in 2000, or 3000) it causes little pain, but I have not been able to convince myself that it has much effect upon the organisms that are present. Stronger solutions are certainly painful, and, it is said, are liable to be followed by hæmaturia.

As a general rule, the bladder after it has been washed out should be left empty. If, however, the surface is inclined to bleed, or if there is much pain, an ounce or two of the solution, or of some indifferent fluid (such as borax or chloride of sodium dissolved in water) may be left behind. It is under these conditions that quinine and iodoform have been especially recommended. I am, however, quite satisfied that in such cases instillation is to be preferred to washing out.

β. Instillation, a method of treatment for which we are indebted mainly to Guyon, consists in injecting slowly, drop by drop, a small quantity of some solution into the neck of the bladder after the bladder has been thoroughly emptied. The best instrument for the purpose is one of Guyon's flexible olivary catheters, with a terminal orifice and a very fine bore. The olive point enables the position of the end of the instrument to be known with accuracy, and the terminal orifice ensures that the solution shall be thrown upon the right spot. A small graduated syringe with a screw-piston should be attached to the other end of the catheter by means of a joint that can be easily detached and cleaned.

This method has the great merit of never causing tension, so that it may be employed in the most acute cases of cystitis, in which washing out is quite inadmissible. It enables an antiseptic, or a sedative of much greater strength than could otherwise be used, to be applied directly to the surface of the mucous membrane. And it deals directly with that part of the bladder in which inflammation nearly always begins, and which, physiologically speaking, is far more active and more important than the rest. So far as recent cases are concerned, and those in which the surface only of the mucous membrane is involved, it has, in my hands, quite superseded the older method of washing out. But when the cystitis has lasted some length of time, and, as so often happens in cases of enlargement of the prostate, the inflammation has spread deeply into the wall, causing it to become immensely thickened and irregular, or when there is a large amount of residual urine, instillation, though still useful as an adjunct, does not meet the requirements sufficiently by itself.

Twenty to thirty drops at a time is the amount I ordinarily employ. This may be injected either into the prostatic portion of the urethra, whence a certain amount will find its way into the neck of the bladder, or directly into the bladder itself. The former is the more usual, as the deep part of the urethra is involved in nearly every case of cystitis and requires as much attention as the bladder itself. As germicides, nitrate of silver (1% to 5%), and corrosive sublimate (1 in 5000 to 1 in 2000) cannot be surpassed. The injections can be felt, but it is very rare for patients to complain of them as causing pain ; and the effect that they exert upon the frequency of micturition and the character of the urine is unmistakable. If the pain is very severe, it may be relieved by the injection of a 10% solution of antipyrin, which should be left in the bladder or by a morphia suppository. Unless the symptoms are very urgent, it is sufficient to repeat the instillation every second day.

Curetting. In obstinate cases of painful cystitis, such as are occasionally met with in women rather late in adult life, Guyon speaks very highly of curetting, provided, of course, no cause can be found in the uterus or any other of the neighbouring organs. The patient is placed under an anæsthetic, the bladder washed out with boric acid or with corrosive sublimate solution, a Volkmann's curette introduced through the urethra (or through a perineal incision in the male sex) and the inner surface of the neck and of the trigone systematically curetted, bit by bit, the forefinger of the left hand being placed in the vagina or the rectum to act as a guide. The rest of the interior of the bladder rarely requires to be touched. The hæmorrhage is said not to be severe. After the operation, the bladder is washed out again, and a catheter tied in, and kept there for some weeks (Camero, *Gaz. Hebd.*, 77, 1896). It is not claimed that the curetting cures the cystitis, but that after the mucous membrane has been thoroughly scraped, and then has been allowed to rest, remedies which were of no effect before often succeed exceedingly well. It remains to be seen whether the number of cases of non-tuberculous cystitis requiring this treatment will not be considerably lessened in the future, now that the use of the cystoscope has become so much more common in the early stages of disease, and the interior of the bladder can be inspected directly, after it has been distended by Kelly's method.

CYSTITIS DUE TO SPECIFIC ORGANISMS.

Inflammation of the bladder is sometimes caused by specific organisms. These may, in certain instances, act by themselves. Much more frequently they are associated with others which are not specific, and it is difficult, if not impossible, to apportion the share to each correctly. The gonococcus, the typhoid bacillus, and the bacillus of tubercle, are all capable of causing cystitis, but it is only the last mentioned that is at all common.

Gonorrhœal Cystitis.

Inflammation of the deep part of the urethra is of frequent occurrence in connection with gonorrhœa, and in a certain proportion of cases spreads upwards and involves the bladder; but the infection is almost always mixed, the ordinary pyogenic organisms being present in addition to the gonococcus. In gonorrhœal cystitis, strictly speaking, no ordinary pyogenic organism should be present, only the gonococcus; no instrument should have been passed; the urine, if drawn with suitable precautions, should remain acid and should give no culture upon gelatin; and the fundus of the bladder, or at least the trigone, should be proved to be inflamed by inspection through the cystoscope. Bumm and Guyon deny the possibility of such an infection; but, although they are rare, several cases that fulfil the required conditions have been recorded by Krogius, Barlow (*Archiv. f. Dermat. und Syph.*, 1892) and Melchior (*Cystite et Infect. Urin.*, Paris, 1895, p. 69). There is no doubt that the epithelium lining the bladder offers a greater amount of resistance to the gonococcus than the columnar epithelium of the urethra, but the resistance is not perfect.

CYSTITIS DUE TO THE BACILLUS OF TYPHOID FEVER.

Inflammation of the bladder is of not uncommon occurrence in connection with typhoid fever, in some cases caused by septic catheters; in others, especially in women, due to the ascent of organisms from the external organs along the urethra into a bladder that is imperfectly emptied. In these cases the ordinary septic organisms of cystitis are present. Krogius, however, (*Ann. des Mal. des Org. Genito-Urin.*, 1894, p. 370), and Melchior (*loc. cit.*, p. 176) have described cases of inflammation of the bladder occurring in typhoid fever, due to the typhoid bacillus itself. There is no question that this organism is capable of passing through the kidneys in typhoid fever if there is the least trace of nephritis, as it has been found in the urine many times; but it is exceedingly difficult to distinguish it under such circumstances from the common bacillus coli. The organism, however, in the case described by Melchior answered the ordinary tests, failing to coagulate milk, or cause the fermentation of lactose, or produce indol; and the patient had not had a catheter passed, and was no longer confined to bed when the attack broke out.

TUBERCULOUS CYSTITIS.

Infection of the bladder by the tubercle bacillus is on the other hand of common occurrence. It may take place at any age. I have seen it in a child four years old and in a man of 70; but it is most frequent in young adult life. It may occur in the course of acute miliary tuberculosis when the symptoms and importance are dwarfed by those of the general infection, or it may be local from the first. And when it is local, it may either be primary, commencing in the bladder itself, or secondary, spreading to the bladder from some of the neighbouring urinary or genital organs.

Primary tuberculosis of the bladder is undoubtedly the more rare of the two. In the majority of instances the affection of the bladder is consecutive to tuberculous disease of the kidneys, or of the epididymis, or of one of the other neighbouring organs. But I am disposed to believe that the proportion of cases in which the bladder is involved by itself has been considerably underrated, especially in the case of women. Since the use of the cystoscope has become more general, and urinary deposits are centrifugalised before being examined under the microscope, the diagnosis of tuberculous ulceration in patients who show no evidence of tuberculous disease elsewhere has become much more common.

Mode of infection. The bladder may be infected either directly through the vesical epithelium, or indirectly through the medium of the blood-vessels and lymphatics.

Of these two methods the former is the more rare. Even in cases of advanced tuberculous ulceration, when numerous fresh points of infection are present upon the surface of the mucous membrane, suggesting from their distribution that inoculation is due to contact, it is more probable that the disease has spread along some of the numerous lymphatics in the mucous and sub-mucous layers. It is doubtful if the tubercle bacillus is pyogenic, so far as the bladder is concerned; and the vesical epithelium, so long as it is uninjured, is an efficient protection. I have known many instances of advanced tuberculous nephritis in which the bladder has remained intact, in spite of the fact that tubercle bacilli had been passing through it in myriads for months together. This, however, does not hold good if there is a calculus, or if the mucous membrane is bruised or injured by injudicious instrumentation, or if some virulent form of septic organism gains access, and acts with the tubercle bacillus. Under these circumstances the protection against infection from the surface is weakened to such an extent that it may fail altogether. Probably this is one of the reasons why tuberculous cystitis is frequently made so much worse by ineffectual local treatment.

Infection ordinarily takes place either through the blood-vessels, or from some neighbouring focus, by extension along the lymphatic capillaries and channels. The arrangement of the latter around the base and neck of the bladder is very complicated; and the course followed by the lymph before it reaches the larger vessels is greatly influenced by the state of physiological activity of the surrounding organs. The lymphatics of the mucous membrane of the pelvis of the kidney, for example, communicate freely with those of the ureter, and these in their turn with those of the sub-mucous plexus of the trigone and the neck of the bladder; and this agrees well with the clinical fact, that in cases of tuberculous pyelitis infection of the bladder often begins around the orifice of the corresponding ureter. In the same way, while the lymphatics from the body of the testis for the most part take a fairly straight route towards the thoracic duct, those from the epididymis are in free communication with the network at the base of the bladder, into which also open the great channels that come from the interior. But considering the extreme frequency of tuberculous epididymitis, and the small number of cases in which the bladder becomes involved, the physiological communication between these organs must be much less free than would be expected from the anatomical arrangement. When infection does take place from the genital organs, it is usually by direct extension from the vesiculæ seminales or prostate. This latter is affected much more frequently and at a much earlier date, judging from the condition of the deposits found in it, than is usually believed.

Pathological changes. Tuberculous disease, whether primary, or due to extension, nearly always begins in the neighbourhood of the neck of the bladder. This may be explained, in part, by the fact that this portion of the bladder is in closer relation with surrounding organs than is the rest. In all cases of primary tuberculosis, however, and probably in a very large proportion of others, the real reason is that this portion of the bladder is the most important physiologically, and has the largest blood-supply. Tubercle bacilli attack it for the same reason that they attack the epiphysial line of a growing bone more frequently than they do the shaft. In comparison with the neck the rest of the bladder is a mere passive receptacle.

The early pathological changes are seldom seen. Tuberculous cystitis soon becomes complicated by septic inflammation and ammoniacal decomposition of the urine. Occasionally it is possible to find a bladder in which there are only a few minute papules projecting slightly above the surface, paler in colour and more translucent than the surrounding mucous membrane. Much more often the surface has already given way, and according to the condition of the urine, whether it is septic or not, there is either a sprouting mass of granulations, flecked here and there with hæmorrhages; or one or more ulcers, irregular in shape with sinuous edges, and bases concealed beneath a mixture of pus, caseous débris and urinary salts.

In the later stages, as the irritability increases, the capacity of the bladder diminishes until it is scarcely capable of holding more than a few ounces of urine. The walls become hard and rigid in places, and soft and yielding in others, so that if any operation is contemplated, it becomes a dangerous matter to distend, or even wash out the bladder. The surface is coated over with an offensive mixture of pus and triple phosphate. The neck is often partly eaten away; and the prostate, the vesiculæ seminales, and the tissues that surround the base of the bladder are infiltrated with caseous deposits or riddled with abscesses.

Symptoms and diagnosis. The symptoms in tuberculous inflammation of the bladder are the same as those of suppurative cystitis—increased frequency of micturition; pain on micturition, referred chiefly to the end of the penis; tenderness on pressure over the bladder; hæmaturia and, sooner or later, pyuria. The blood, as a rule, makes its appearance in the urine at an early period in the disease, and is more or less constantly present throughout. Nearly always, as might be expected from the situation of the disease, it comes at the end of micturition, when the pain is most severe. The amount of pus depends upon the severity of the septic inflammation.

The chief characteristic, however, of tuberculous cystitis is not so much the actual symptoms, or the order in which they follow, as their apparent causelessness. Either they set in without its being possible to assign a sufficient reason for them; or if there is such a reason, if as not uncommonly happens, the tuberculous inflammation is consecutive to an attack of gonorrhœa, they persist long after the apparent cause is past and gone. Inflammation of the bladder, beginning without a definite exciting cause, or persisting in spite of ordinary remedies should always excite the gravest suspicion, especially when the patient is young and in any way predisposed to tubercle.

In the later stages, the symptoms are the same in kind, but infinitely more severe. There are very few complaints in which strangury is more acute and less amenable to treatment, than in tuberculous cystitis. As the ulceration involves the neck, and the urine becomes ammoniacal, micturition is incessant, day and night, and accompanied by the most agonising pain. Neighbouring organs become involved. Septic pyelitis sets in. The kidneys become affected by suppurative nephritis. Abscesses and fistulæ form around the neck of the bladder. The urine drains away continuously, without giving the slightest relief from the pain; and at last the patient's strength and endurance are absolutely worn out.

The diagnosis of tuberculous cystitis in its early stages can only be made certain by the use of the cystoscope and the discovery of tubercle bacilli in the urine. The former detects the ulceration : the latter shows the cause. A thorough examination of both the bladder and the urine should be made in every case of cystitis that either begins without a definite cause, or persists in spite of treatment, especially if the patient is young. It is true that the bladder in tuberculous cystitis resents the use of instruments ; and that even with the greatest care, the inflammation is often made worse, temporarily, by examination ; but without the use of the cystoscope it is impossible to be certain as to the existence of ulceration, or to know anything of its position or extent ; and this knowledge is essential.

For the discovery of tubercle bacilli in the urine, it is necessary that the deposit should be collected by means of a centrifugal machine within an hour or two of the urine being passed. The bacilli are never very abundant (when the tubercle is limited to the bladder) and a negative result, if the urine is allowed to stand for some hours in a conical glass and the sediment collected by deposition, is worth nothing. Care must be taken that the bacillus of smegma is not mistaken for that of tubercle. To avoid doubt, it is advisable to make use of Melchior's catheter.

The diagnosis of tuberculous ulceration alone is not sufficient. It is essential to determine as early as possible whether it is primary and limited to the bladder, or secondary to some deposit elsewhere. The epididymis, the prostate and the vesiculæ seminales are accessible more or less to direct examination ; the kidneys which are equally important in this respect, are not; and especially when the ulceration is near the orifice of one of the ureters, it is very difficult to prove that the pelvis of the kidney is not affected. It is my impression that when the orifice is actually involved, pyelitis is nearly always present.

The absence of renal pain and renal colic, and of any unusual degree of tenderness or pressure over the renal region, is of no value. It is perfectly consistent with the early stages of tuberculous pyelitis. There is nothing to be learnt from the urine as it comes from the urethra, unless the disease is far advanced. In one or two instances the urine coming from one of the ureters has been seen through the cystoscope to be cloudy from pus as it entered the bladder; but unless, again, the disease is far advanced, this must be regarded as quite exceptional. There is more hope from passing a catheter up the suspected ureter, and obtaining a specimen of the urine directly as it comes from the kidney. In women this can be accomplished without seriously bruising the mucous membrane (a thing to be carefully avoided in all cases, but especially in the neighbourhood of tuberculous infection), by placing the patient in the lithotomy position, under an anæsthetic, dilating the urethra, and introducing a suitable speculum into the bladder. Some assistance can be obtained from the presence of the forefinger in the vagina, as the ureter can be felt, and the orifice pushed upwards into the bladder to meet the catheter. I have succeeded in this on several occasions, and have not found that it was followed by incontinence or any other ill-effect; but it should not be attempted unless the mucous membrane around the orifice is healthy. With men it is very different. The only method is by the combined cystoscope and ureteral catheter; and although W. Meyer (New York Academy of Medicine, April, 1897) claims never to have failed but once, when the orifice of the ureter was contracted, others have found the proceeding one of extreme difficulty.

The ureters have been catheterised through a suprapubic incision; but a very wide one is required, and this manifestly is inadvisable for mere purposes of diagnosis.

Later, when the kidney itself is involved and the urine is persistently of low specific gravity, and contains an amount of pus that is excessive in proportion to the extent of the vesical ulceration, there is little or no difficulty.

Treatment. In every case of tuberculous cystitis, whether primary or consecutive to tuberculous disease of neighbouring organs, I attach the greatest importance to constitutional measures. I am strongly of opinion that in all incipient cases they should be given a thorough trial before any active local treatment is adopted. I refer not so much to cod liver oil and iron, though these in their way are good, as to abundance of fresh air and especially sea-air. I have known many cases of undoubted tuberculous disease of the urinary organs improve beyond all that could have been expected and some recover entirely, simply I believe from their being made to live in the open air or sent on long sea voyages. It is true that other measures were not neglected at the same time, but these had been tried as fully before without producing any marked effect. Later, when the tuberculous process has taken firm hold, and especially when it has become complicated by suppurative cystitis and pyelitis, very much less of course is to be expected. It is no good sending such cases away from home.

As a general rule local medication in tuberculous cystitis does more harm than good. Iodoform, lactic acid, and the other drugs that have been recommended, chiefly on account of the way in which they influence the tuberculous process in other organs, never reach the structures upon which they are intended to act. And the risk of introducing pyogenic organisms and setting up septic cystitis in addition is immensely increased. The only exception that I am disposed to make is in favour of a very dilute solution of corrosive sublimate. This may sometimes be injected with benefit, but I am rather disposed to think that the good it does is almost entirely due to the effect that it has in checking incipient septic inflammation.

Intestinal antiseptics are of very little service. Carbonate of guaiacol, in cachets containing seven to ten grains, seems to be beneficial sometimes, and is certainly less irritating than creosote. It passes through the stomach unaltered and is decomposed in the intestine, the guaiacol making its appearance in the urine. In the later stages when the pain and strangury become severe, sedatives are absolutely essential. Morphia is the only one that can be relied upon, and even this, unless it is pushed, only gives partial relief. In these cases there is little fear of creating a morphia habit. It is no use injecting it into the bladder; it must be given hypodermically or as a suppository.

Much has been hoped from drainage of the bladder, so as to give it complete physiological rest. In some instances it does relieve the strangury, but they are the minority, and it has very little influence upon the general course of the disease. I have found the supra-pubic method the more useful of the two. The bladder can be kept empty without interfering with its most sensitive portion; a convenient apparatus can be worn, and septic inflammation can be kept in check. But it seldom relieves the pain altogether; the tube requires the nicest adjustment, or it may make the strangury worse, and if the disease is far advanced and the size of the bladder is much reduced, it is by no means easy to carry out properly. With perineal drainage I have been less successful. The wound seems to become infected at once, and the ulceration to spread all the more rapidly. This, however, may have been accidental and due to the locality of the disease, as in some cases it is reported to have answered well.

Drainage of the bladder is useful in another way. It enables local treatment to be carried out more effectually and with better results. If there is a free artificial opening to the bladder, there is no risk of making the inflammation worse by causing tension, and even washing out the bladder is sometimes beneficial. Certainly it is much more easy to keep septic inflammation from breaking out and intensifying the tuberculous process.

Iodoform may be used either as a powder by insufflation into the empty bladder through a supra-pubic cannula, or as an emulsion in glycerin. Some small portion in either case is thrown down upon the mucous membrane and brought into contact with the ulcerated surface. Aristol may be used in the same way, or dissolved in parolein. Guyon speaks highly of a five per cent. solution of antipyrin, and of guaiacol combined with iodoform in the proportion of five parts of guaiacol and one of iodoform, dissolved in one hundred parts of sterilised olive oil. Not more than thirty grains of guaiacol should be injected in the course of twenty-four hours.

Strong solutions of nitrate of silver may sometimes be used with advantage. In cases in which the interior is covered with vascular and gelatinous looking granulations, Jacobson recommends swabbing the surface over with a solution so strong as 120 grains to the ounce. If the pain this causes is severe, it may be relieved by the injection of sodium chloride solution afterwards.

In a few instances an attempt has been made to procure relief by abrogating the function of the bladder entirely, draining it both supra pubes and through the perineum. In one case of advanced disease in which the bladder was very much contracted, this succeeded fairly well for a time (Bolton Bangs, *Jour. of Cut. and Gen. Urin. Dis.*, 1892, p. 173), and in another in which the supra-pubic opening was allowed to close after some weeks, the severity of the pain did not recur.

These are at best but palliative measures, and when the disease is far advanced, or when other organs are seriously involved, they are the only ones admissible. Any attempt at complete removal is hopeless, and will do more harm than good. But if the diagnosis is made sufficiently early, and the disease is either primary, beginning in the bladder, or if consecutive, in some organ such as an epididymis that admits of active local treatment, this no longer holds good. Complete removal is possible and is certainly to be preferred.

Constitutional measures should be given a fair trial first. But if the disease is limited to the bladder and shows signs of spreading to regions (such as the orifice of a ureter) that would make complete removal questionable ; or if at the end of three months, after living under the best conditions that the patient can afford, there is no definite improvement, I am convinced not only that the attempt is justifiable, but that it should be made without further delay. There is nothing to be gained by waiting, and there is now a sufficient number of cases on record of patients, who have remained well for four years and even longer after the operation, to prove that there is a reasonable hope of effecting a permanent cure, without undue risk. Everything depends upon early and accurate diagnosis. It is for this reason that the use of the cystoscope and the careful examination of the urinary deposit should be insisted upon in every case in which there is the least ground for suspicion.

Those cases are the most suitable in which the disease begins in and is still limited to the bladder ; but in several instances in which other organs have been involved, the patients, if they have not been absolutely cured by the operation, have certainly derived benefit from its performance.

In women tuberculous nodules and ulcers can sometimes be scraped out with a curette through the urethra, after this has been dilated. But supra-pubic cystotomy, as performed now-a-days, is so simple and so safe, and allows the interior of the bladder to be inspected so thoroughly while the curetting is actually being done, that it should always be preferred, unless the disease is of the most limited character.

According to Reverdin (*Ann. des Mal. des Org. Gen.*

Urin., 1889, p. 263) who gives a very complete summary of the earlier cases, the credit of deliberately opening the bladder with the view of dealing with tuberculous disease belongs to Guyon. Iversen, Schatz, and Trendelenburg, who had already performed this operation (the last mentioned on three occasions) had been led to open the bladder for other reasons. Since then more than twenty cases have been recorded by different observers.

The methods employed vary according to the conditions that are found. The bladder must be opened so that the interior can be inspected thoroughly. This can only be done through a supra-pubic incision, and only so long as the walls of the bladder retain their elasticity. When they have become rigid, and the cavity has contracted, it is no longer practicable. At least one case of rupture has been recorded. The perineal route, and Howard Kelly's method of air distension in women, are rarely of any use.

The most suitable cases are those in which there are only one or two ulcers upon the trigone. These should be scraped thoroughly with a curette, and then either sponged over with a solution of chloride of zinc, gr. xxx. ad ℥j. (Battle) or, as I prefer, touched with Paquelin's cautery. If the ulcerated surface lies against the symphysis, so that it cannot be seen, the curette can be guided almost as well by the finger, and after the soft structures have been scraped away, iodoform should be well rubbed in. Those cases in which a large portion of the bladder surface is covered with flabby granulations should be treated in the same way, the hæmorrhage being checked by the injection of hot water, or by the cautery. In several instances in which this has not sufficed the bladder has been packed with iodoform gauze. When the whole surface is studded with minute granulations, and it is evident that the disease has spread all over the bladder, it is questionable if interference can lead to any good. In three cases Bardenheuer (*Central.*

f. Gynækol., 14, 1894) dissected away the whole mucous membrane. A certain amount of reproduction of the epithelial surface took place, spreading from the ureters and the orifice; but in spite of this the cavity contracted until it was almost obliterated, and complete incontinence followed.

Drainage should be kept up for some days or even weeks, in order to keep the bladder at rest and give the wounds the best chance of healing.

I have operated myself on three occasions. The first was in January, 1894. The patient had been suffering from cystitis for upwards of three years. Recently the urine had become ammoniacal. Several ulcers, coated over with a mixture of phosphates, pus, and caseous debris were found around the neck. These were scraped and cauterised, some iodoform being rubbed in afterwards. The bladder was drained for a few days. The wound healed in three weeks. The symptoms were almost completely relieved; and though the patient has generally to rise once at night there has been no recurrence, and her general health is perfectly satisfactory. In another operated upon two years ago, the bladder was opened a second time, a few months after the first, owing to a recurrence of the symptoms; but the patient, a boy twelve years of age, has remained well since. The third is too recent to be of value.

Two other cases have been reported in England by Battle (*Clinical Society's Transactions*, 1890, and *Lancet*, 1895, vol. ii., p. 1165). The former appears to have been cured; five years later there was no recurrence, and the patient continued in good health. Many others have been performed abroad.

In some of these the disease was not limited to the bladder. Reverdin's patient, for example, had suffered two years before from tuberculous epididymitis, and was well two years after the operation in spite of a perinephritic abscess (*Ann. des Mal. des Org. Gen. Urin.*, 1889, p. 263).

Greiffenhagen's (*Deutsch Zeit. f. Chirurgie*, 43, p. 280) had a caseous abscess pointing in the perineum, probably starting in connection with the vesiculæ seminales. And Bell (*Journal of Cut. and Gen. Urin. Diseases*, August, 1892) records another in which, in spite of the presence of tuberculous epididymitis, the bladder symptoms almost disappeared after the ulcers had been scraped with a Volkmann's spoon and cauterised. Two years later, when the testis was removed, the man was well, with the exception of some incontinence of urine.

It is true that some cases in which radical operations have been performed have relapsed; that some have not benefited by the operation at all; and that the benefit experienced by others may have been due in part to the drainage. It is admittedly an operation that is only likely to be successful in a minority of cases of tuberculous cystitis; and should never be attempted when the disease is advanced, and the bladder is rigid and contracted. The important point is that, thanks to better and more accurate methods of diagnosis, cases for which it is suited, if they are seen in time, can be separated out from the rest; and if the operation is performed while it is still possible to remove the whole of the disease, there is a reasonable hope of effecting a permanent cure from a most distressing complaint, without exposing the patient to any undue risk.

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